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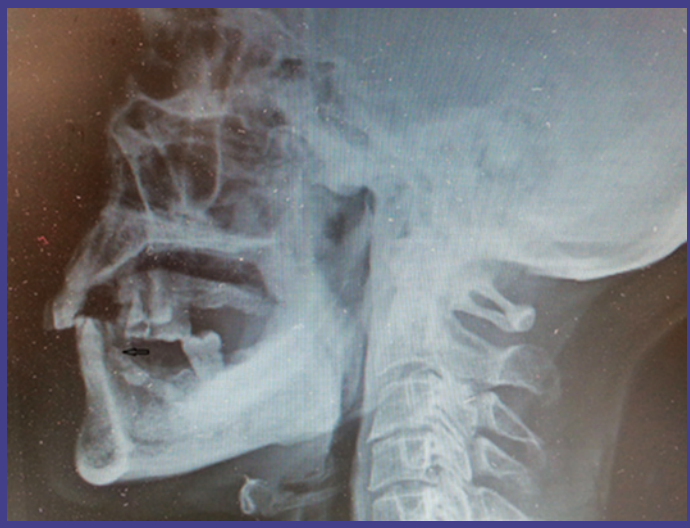

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Complementary and Alternative Medicine Use in Lung Cancer Patients and Its Impact on the Quality of Life

Akciğer Kanseri Hastalarında Tamamlayıcı ve Alternatif Tedavi Kullanımı ve Yaşam Kalitesi Üstüne Etkileri

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ABSTRACT

AIM: *In this study we aimed to provide data about the rate of complementary and alternative medicine use among lung cancer patients and the effect of the intervention on the quality of life.*

METHODS: *The study population consisted of patients visited the oncology outpatient clinic of Yedikule Chest Diseases Training and Research Hospital to receive ambulatory chemotherapy between December 2011 and March 2012 (N=200). Data was collected using the Personal Information Form, the Complementary and Alternative Medicine Approaches Scale and the Nightingale Symptom Assessment Scale. The data obtained from the patients using complementary and alternative medicine was compared with others using Independent Sample T Test, Mann-Whitney U and the Chi-square Test.*

RESULTS: *The mean age of participants was 59.97±8.41 (min28-max84) and 81% of them were male. Complementary and alternative medicine was used by 56.5% of the patients. The most preferred Cognitive-Behavioural Therapy and Manipulative Approaches were praying (89%), performing salat (95%), laughing (82%), visiting a neighbour (78%) and dancing (54%). The most preferred herbal approaches were linden tea (81%), green tea(74%), thyme(70%), sage (67%), and grape seed crust(67%). Most used nutritional approaches were fruits-vegetables-fish-chicken-yogurt (100%), carrots (98%), garlic (97%), pomegranat(93%), meat (92%), pastry and milky desserts (91%). The rationale for using complementary and alternative medicine were feeling psychologically relaxed (81%) and believing that they would increase the effect of treatment (65%).*

CONCLUSION: *Complementary and alternative medicine use is very common among lung cancer patients in Turkey and it seems that the practice increases the quality of life of the patients.*

Key words: *alternative medicine; complementary therapies; lung neoplasms; quality of life*

ÖZET

AMAÇ: *Bu çalışmada akciğer kanseri olan hastalarda tamamlayıcı ve alternatif tıp kullanımı üzerine veri sağlamayı ve bunun yaşam kalitesi üzerine etkilerini araştırmayı amaçladık.*

YÖNTEM: *Çalışma evreni Yedikule Eğitim ve Araştırma Hastanesi Onkoloji Polikliniğine, Aralık 2011 ve Mart 2012 arasında kemoterapi almak için başvuran hastalardan oluştu (N=200). Veriler bireysel bilgi formu, tamamlayıcı ve alternatif tıp yaklaşım skalası ve Nightingale belirti belirleme skalası kullanılarak toplandı. Tamamlayıcı ve alternatif tıp yaklaşım kullanan katılımcılar ile kullanmayanların verileri bağımsız değişkenler T testi, Mann-Whitney U testi, ve ki kare testi kullanılarak karşılaştırıldı.*

BULGULAR: *Çalışmaya katılanların yaş ortalaması 59,97±8,41 yıldı (min 28-max 84) ve %81'i erkekti. Tamamlayıcı ve alternatif tıp %56,5 hasta tarafından kullanılıyordu. Bilişsel-Davranışsal Terapiler ve Manipulatif Yaklaşımlardan en fazla dua etme (%95), namaz kılma (%89), gülme (%82), komşuya gitme (%78) dans etme (%54) tercih ediliyordu. Bitkisel yaklaşımlardan; ıhlamur çayı (%81), yeşilçay (%74), kekik (%70), adaçayı (%67), üzüm çekirdeği kabuğu (%67); besinsel yaklaşımlardan meyve-sebze-balık-tavuk-yoğurt (%100), havuç (%98), sarımsak (%97), nar (%93), hamur ve sütlü tatlı (%91), kırmızı et (%92) tercih ediliyordu. Kullanma nedenleri, psikolojik olarak rahatlamak (%81) ve tedavinin etkisini arttırdığını düşünmek (%65) olduğu görüldü. Tamamlayıcı ve alternatif tedavi kullanma sebepleri içerisinde en sık sebep psikolojik rahatlama (%81) ve tedavi etkinliğini artırmaktı (%65).*

SONUÇ: *Türkiye'de akciğer kanseri olan bireyler arasında tamamlayıcı ve alternatif tıp kullanımı oldukça yaygındır ve uygulama ile yaşam kalitesi artıyor gibi gözükmektedir.*

Anahtar kelimeler: *alternatif tıp; tamamlayıcı tıp; akciğer kanseri; yaşam kalitesi*

Introduction

Lung cancer is one of the most important diseases of the respiratory system. Although it was a rare disease at the beginning of the 20th century, cigarette smoking increased its incidence and it has become the most common cancer in the world.

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Lung cancer negatively affects the bio-physiological, psychological and socio-cultural aspects of an individual's life. The disease is mostly diagnosed at advanced stages and chemotherapy is frequently used in the treatment. In patients treated with chemotherapy, the quality of life is disrupted and the patients often need to use complementary and alternative treatments (CAM)[1,2].

CAM are health care products and procedures that have not been considered as the components of conventional medicine, yet. Complementary treatments are used to support scientific medicine. They are commonly used to improve the quality of life, to decrease the symptoms and side effects of medicine and to provide physical and psychological support. Alternative treatments are performed instead of medical treatment and their effects are not scientifically proven[1,2].

Nowadays the frequency of CAM use is gradually increasing both in the general population and also among cancer patients. This is because CAM resolves the symptoms of cancer and the side effects of treatment, supports the immune system and increases the quality of life. Patients experience methods like herbal mixtures, vitamins, antioxidants, yoga, meditation, bio-energy, acupuncture, aromatherapy or religious practices[3].

The use of CAM differs according to the geographic location of the country, ethnicity, education, socio-economic factors and religious beliefs. The most commonly used CAM methods in western countries are multivitamins, meditation, hypnotherapy, relaxation exercises and aromatherapy; and in eastern countries herbal mixtures are more common. In the study conducted by Akyürek et al. 58.5% of the patients used herbal mixtures consisting of stinging nettles and its seeds. Many of the patients ignore to inform the health care providers about the use of CAM. Patients must be interrogated about the use of CAM[3,4].

Although there a few studies dealing with CAM use, the issue has not been studied well in our country [1,3,5-9]. In this study we aimed to provide data about the rate of CAM use among lung cancer patients and the effect of the intervention on the quality of life.

Methods

This study was planned as a definitive study to identify the frequency of the use of complementary and alternative treatment in individuals with lung cancer and its association with the quality of life. The study questions are:

- What are the CAM use approaches and reasons of use in individuals with lung cancer?
- Does CAM use improve quality of life?

Settings and Patients

The population of the study consists of patients that applied to the Oncology Department of Yedikule Chest Diseases Training and Research Hospital for ambulatory chemotherapy between December 2011 and March 2012 (N=200).

The inclusion criteria were: being 18 years of age or older, not being in the terminal stage, being open to communication and collaboration, being diagnosed with cancer at least two months ago and being treated with chemotherapy and/or radiotherapy.

Data Collection Tools

The data was collected using the Personal Information Form that covered the socio-demographic characteristics of the individuals, the Complementary and Alternative Medicine Approach Scale and the Nightingale Symptom Evaluation Scale.

Personal Information Form

It included questions about the individual's socio-demographic characteristics, the diseases and the use of complementary and alternative treatments.

Complementary and Alternative Medicine Approach Scale (CAMAS)

It was developed by Can et al. (2009) with the purpose of identifying the complementary and alternative treatment use approaches and reasons of people with cancer. The scale consists of 55 topics and three sub-groups. The sub-groups contain cognitive, behavioural and manipulative; herbal and nutritional interventions. The scale points can be calculated by giving "0" points if the patient does not use or perform interventions (never or stopped) and "1" point for using and performing interventions (sometimes, often, all the time, I started, I decreased, I increased, I continued just the same). The Cronbach Alpha coefficient was calculated as 0.80 for herbal approaches, 0.85 for the nutritional approach, 0.49 for the cognitive-behavioural and manipulative approach and 0.85 for the entire scale[7].

Nightingale Symptom Assessment Evaluation Scale (N-SAS)

It is a quality of life scale developed in 2009 for cancer patients by Can and Aydıner. The scale consists of 38 items and three sub-scales: physical wellbeing, social wellbeing and psychological wellbeing. This Likert type scale is scored by giving "0" points for the answer 'no', "1" for the answer 'a little', "2" for 'not much', "3" for 'a lot' and "4" for 'too much'. High scores indicate that patients are affected highly by the problems caused by the disease/treatment and that the general quality of life is poor. Quality of life is determined as "very good" if the scores are between 0-0.50, "good" if the scores are between 0.51-1.50, "moderate" if the scores are between 1.51-2.50, "poor" if the scores are between 2.51-3.50 and "very poor" if the scores are between 3.51-4.00. In a study conducted by Can (2008) the validity and credibility of the N-SAS was tested and the Cronbach Alpha coefficient was identified between 0.81-0.87[7].

Ethical Considerations

Before the study was started written permission was obtained from the Yedikule Chest Diseases and Surgery Training and Research Hospital and the Health Directorate of Istanbul. The individuals comprising the study sample were explained the purpose of the study and what was expected of them, and informed consent was obtained in accordance with principles of willingness and volunteering to participate in the study.

The Limitations of the Study

The study sample included patients applying to one hospital only. Thus, the results of this study cannot be generalized.

The Evaluation of the Data

The SPSS for Windows 21.0 package program was used for the statistical analyses of the data obtained in the study. To evaluate the study data, definitive statistical methods (rate, mean, standard deviation, and frequency values) were used. To evaluate the quantitative data the independent sample t-test and the Mann-Whitney U tests were used. The chi-square test was used in the analyses of qualitative data. Distribution of the variables was checked using the Kolmogorov-Smirnov test. The significance of the p value was accepted <0.05.

Results

The mean age of the individuals included in the study was 59.97±8.41 (min 28-max 84). A total of 113 (56.5%) participants used CAM. Demographic data of the participants and CAM use ratios were summarized in Table 1 and 2. Younger, married and unemployed patients were frequently the CAM users (p>0.05). Gender, education, profession, income, chronic diseases and chemotherapy did not affect the CAM use rates. Family history of tumours, undergoing radiotherapy and surgery lowered CAM use ratio (p<0.05).

As cognitive-behavioural therapies and manipulative approaches, the participants mostly preferred praying (95%), performing the five daily prayers (89%) (namaz/salat) and laughing (82%). Among herbal approaches the most common choices were linden tea (81%), green tea (74%) and thyme (70%). The most common nutritional supplements were fruits (100%), vegetables (100%) and fish (100%). Table 3 summarized the CAM types used by the participants.

The rationale to use cognitive-behavioural therapies and manipulative approaches were mostly psychological relief (81%, n=91), praying (79%, n=89) and not leaving any methods untried (5%, n=6). The rationale of using herbal approaches were to increase the efficacy of treatment (65%, n=47), to increase blood values (61%, n=69), to strengthen the immune system (42%, n=47) and not to leave any methods untried (5%, n=6). The rationale of using nutritional approaches were to increase the efficacy of treatment (77%, n=87), to prevent the progression of the diseases (45%, n=51), to strengthen the immune system (35%, n=39) and to increase the appetite (7%, n=8). The rationales of CAM use was summarized in Table 4.

The Nightingale Symptom Assessment Scale total mean scores were 2.51 ± 0.96 (poor) in all individuals, 1.91±0.61 (moderate) in CAM users and 3.25±0.72 (poor) in non-CAM users. Among the subscales of the Nightingale Symptom Assessment Scale the mean physical wellbeing scores were 2.44±0.93 (moderate) in all individuals, 1.93±0.73 (moderate) in CAM users and 3.12±0.71 (poor) in non-CAM users.

Social wellbeing scores were 1.82±1.34 (moderate) in all individuals, 1.14±0.83 (good) in CAM users and 2.83±1.14 (poor) in non-CAM users, the psychological wellbeing mean scores were 3.24±0.72 (poor) in all individuals, 2.85±0.65 (poor) in CAM users and

3.74±0.58 (very poor) in non-CAM users. The total mean Nightingale Symptom Assessment Scale scores of CAM users (Z=-10.05, p<0.001) and the physical wellbeing (Z=-9.52, p<0.001), social wellbeing (Z=-9.49 p<0.001) and psychological wellbeing (Z=-8.56 p<0.001) mean subscale scores were statistically significantly lower that the mean scores of non-CAM users (Table 5).

Table 1. *Demographic characteristics of lung cancer patients and the effect of complementary and alternative medicine use*

CAM use		**Yes (n=113)**	**No (n=87)**	**Total**		
N=200		n (%)	n (%)	n (%)	**X² / t**	**P value**
Age	18-60	70 (54.3)	36 (45.7)	106 (53.0)	t=-4.04	<0.001
	>60	43 (45.7)	51 (54.3)	94 (47.0)		
Gender	Male	95 (58.6)	67 (41.4)	162 (81.0)	x²=1.59	0.207
	Female	18 (47.4)	20 (52.6)	38 (19.0)		
Marital status	Married	111 (59.4)	76 (40.6)	187 (93.5)	x²=9.56	0.002
	Single	2 (15.4)	11 (84.6)	13 (6.5)		
Education	Illiterate	9 (39.1)	14 (60.9)	23 (11.5)	x²=5.85	0.211
	Primary school	65 (57.0)	49 (43.0)	114 (57.0)		
	Middle school	17 (73.9)	6 (26.1)	23 (11.5)		
	High school	16 (53.3)	14 (46.7)	30 (15.0)		
	University	6 (60.0)	4 (40.0)	10 (5.0)		
Occupation	Housewife	13 (43.3)	17 (56.7)	30 (15.0)	x²=9.39	0.052
	Worker	15 (88.2)	2 (11.8)	17 (8.0)		
	Government employee	4 (50.0)	4 (50.0)	8 (4.0)		
	Self-employment	25 (56.8)	19 (43.2)	44 (22.0)		
	Retired	53 (54.1)	45 (45.9)	98 (49.0)		
	Other	3 (100)	0 (0.0)	3 (1.5)		
Income level	Ends Meet	69 (53.5)	60 (46.5)	129 (64.5)	x²=1.34	0.247
	Ends don't meet	44 (62.0)	27 (38.0)	71 (35.5)		
Employment status	Employed	15 (93.8)	1 (6.3)	16 (8.0)	x²=9.82	0.002
	Not employed	98 (53.3)	86 (46.7)	184 (92.0)		
Health insurance	Insured	111 (56.6)	85 (43.4)	196 (98.0)	x²=0.07	1.000
	Uninsured	2 (50.0)	2 (50.0)	4 (2.0)		

x² Chi Square test / t Independent samples t test, CAM: complementary and alternative medicine

Table 2. *The relation between some characteristics of lung cancer patients and complementary and alternative medicine use*

CAM use		**Yes (n=113)**	**No (n=87)**	**Total**		
N=200		n (%)	n (%)	n (%)	**X² / t**	**P value**
Chronic Disease	Healty	78 (57.4)	58 (42.6)	136 (68.0)	0.13	0.723
	Hypertension	17 (58.6)	12 (41.4)	29 (14.5)		
	Diabetes Mellitus	13 (50.0)	13 (50.0)	26 (13.0)		
	Benign Prostate Hyperplasia	1 (20.0)	4 (80.0)	5 (2.5)		
	Heart Failure	4 (100)	0 (0.0)	4 (2.0)		
Cancer in family members	Yes	15 (34.9)	28 (65.1)	43 (21.5)	10.41	0.001
	No	98 (62.4)	59 (37.6)	157 (78.5)		
Surgical therapy	Yes	18 (35.3)	33 (64.7)	51 (25.5)	12.53	<0.001
	No	95 (63.8)	54 (36.2)	149 (74.5)		
Radiation therapy	Yes	54 (43.9)	69 (56.1)	123 (61.5)	20.63	<0.001
	No	59 (76.6)	18 (23.4)	77 (38.5)		
Chemotherapy	Yes	112 (56.3)	87 (43.7)	199 (99.5)	0.77	1.000
	No	1 (100)	0 (0.0)	1 (0.5)		

x² Chi Square test / t Independent samples t test, CAM: complementary and alternative medicine

Table 3. *Complementary and alternative medicine types used by lung cancer patients (N=113)*

Cognitive-Behavioral Manipulative Supplements		**Herbal Supplements**		**Dietary Supplements**	
	n (%)		n (%)		n (%)
Pray	107 (95)	Linden tea	91 (81)	Fruits	113 (100)
Namaz	100 (89)	Green tea	85 (74)	Vegetables	113 (100)
Laugh	93 (82)	Thyme	79 (70)	Fish	113 (100)
Visit the neighbors	88 (78)	Sage tea	75 (67)	Yogurt	113 (100)
Dancing	61 (54)	Grape seed and peel	75 (67)	Chicken	113 (100)
Massage	53 (36)	Rosehip tea	49 (44)	Carrot	111 (98)
Being prayed by hodja	39 (33)	Ginger	48 (43)	Garlic	109 (97)
Visit place where holy man is buried	21 (19)	Nigella sativa	48 (43)	Pomegranate	106 (93)
Exercise	17 (16)	Vitamin	47 (42)	Meat	104 (92)
Lead	12 (11)	Grape seed extract	37 (33)	Sweet	102 (91)
Carry written Amulet	9 (8)	Linseed	36 (32)	Milk and milk products	101 (89)
Foot massage	9 (8)	Turmeric	32 (28)	Bread/pastry	91 (81)
Take a vow	9 (8)	Bee polen	32 (28)	Honey	88 (79)
Paint	8 (7)	Blueberries	31 (27)	Boiled mulberry juice	76 (67)
Cup pulling	3 (3)	Stinging nettle	30 (26)	Boiled harnup juice	40 (35)
Acupressure	2 (2)	Chmomile	16 (15)	Chestnut honey	21 (19)
Meditation	2 (2)	Almond	13 (12)	Anzer honey	19 (17)
		Ginseng panex	6 (5)	Pomegranate juice	19 (17)
		Hypericum perforatum	3 (3)		

Table 4. *Rationale for complementary and alternative medicine use among lung cancer patients (N=113)*

	N (%)
Cognitive-Behavioral Manipulative Supplement	
To feel better emotionally	91 (81)
Religious practices	89 (79)
Feeling hopeless and seek help	6 (5)
Herbal Supplement Subgroup	
To increase the effect of therapy	74 (65)
To raise blood values	69 (61)
To strengthen the immune system	47 (42)
Feeling hopeless and seek help	6 (5)
Dietary Supplement Subgroup	
To increase the effect of therapy	87 (77)
To stop the progression of the disease	51 (45)
To strengthen the immune system	39 (35)
To increase the appetite	8 (7)

Discussion

The use of CAM in cancer is gradually increasing and its frequency has been reported between 7% and 64% (average of 31.4%)[10]. In a study conducted in 14 European countries including Turkey, it was reported that the use of CAM was 36% in patients with cancer and it was used in a very wide range between 15%-73%[11]. Kav et al. have reviewed the studies carried out in Turkey between 1999-2007 and have reported that the main frequency of CAM use was 46.2% and ranged between 22.1% and 84.1%.[6] Çetin, Kurt, Erbaycu et al. and Can et al reported that 60%, 48.8%, 78.6% and 71.5% of the patients use alternative treatment at least once after being diagnosed[7,9,12,13]. Similarly, 56.5% (n=33) of the patients in our study were also using CAM. It can be

Table 5. *Comparison of the quality of life of lung cancer patients (N=200)**

	Complementary and alternative medicine users and non-users				
	Users (n=113)	Non-users (n=87)	Total		
	Mean ± SD (Median)	Mean ± SD (Median)	Mean ± SD	Z	P
Total score	1.91±0.61 (0.82)	3.25±0.72 (0.80)	2.51±0.96	10.05	<0.001
Physical Wellbeing	1.93±0.73 (0.80)	3.12±0.71 (1.01)	2.44±0.93	-9.52	<0.001
Social Wellbeing	1.14±0.83 (0.90)	2.83±1.14 (0.99)	1.82±1.34	-9.49	<0.001
Psychological Wellbeing	2.85±0.65 (1.31)	3.74±0.58 (0.66)	3.24±0.75	-8.56	<0.001

*Nightingale Symptom Assessment Scale, z Mann-whitney u test

expressed that this rate is rather high when compared to other countries.

The incidence of lung cancer increases with age due to various factors[2,3]. In our study the mean age of the patients was 59.97±8.41 (min 28-max 84) and CAM use was significantly higher in individuals aged between 18 and 60 than in the individuals over 61 (t=-4.04, p<0.001). It was thought that use of social media more frequently by young individuals influenced the result.

Lung cancer is seen more often in smoking and hard working men[7,9,14]. In our study 81% of the individuals were male, and CAM use was more frequent in males. Similarly Erbaycu et al., Algıer et al., Akyürek et al. and Araz et al. have reported that CAM use was more frequent in male patients[3,9,15,16].

Our study contained mostly the unemployed males (92%) and CAM use was significantly higher in unemployed patients (p<0.05). This result resembles the results obtained by Akyürek et. al, Can et al., Erbaycu et al., Güngörmüş and Çetin et al. [3,7,9,12,17]. The frequent use of CAM in these aforementioned groups may be related to the will to reach results in shorter durations, the fact that this group is more susceptible to environmental influence and the increased popularity of CAM in recent years.

In the studies conducted in our country it was stressed that religious practices were the prominent type of CAM approaches. Literary, studies have shown that cancer patients pray more often than patients with other chronic diseases. Studies have also shown that praying was effective in decreasing stress and anxiety, increasing positive attitudes and desire to live[18,19]. It was thought that individuals turn towards religious practices because of the fear of death.

Laughing is a treatment method that dates back to ancient ages. In an article published in the journal of Pediatric Oncology Nursing (2003), it has been stressed that laughter had an important role in supportive treatment to reduce the stress of children with cancer[18]. From this point of view it was pleasing that 82% of our patients used laughing.

Linden tea soothes nerves and regulates blood circulation. The polyphenols in green tea may reduce the risk for prostate, breast, esophageal, lung and bladder cancers. Grape seeds are used in prevention from cancer, peripheral venous insufficiency, respiratory tract diseases and to strength the immune system[18]. These herbal products are used frequently because information about their beneficial uses are broadcasted frequently in media. In addition, their hematinic and immune system strengthening effects are known and they are relatively cheap and easily accessible.

When we reviewed previously conducted studies, Uğurluer et al. reported that 89.6% of the individuals had tried and used stinging nettles at least once, Taş et al. reported the rate as 88%, Akyürek et al. as 59% and Erbaycu et al. as 50.2%[2,3,9,19]. In our study it was seen that 74% of the patients had never used stinging nettles. Recently, news has been broadcasted in media that stinging nettles have harmful effects during chemotherapy. These broadcast might have decreased the use of stinging nettles.

In our study, 42% of the patients stated that they had started using vitamins. This result is similar with the results of other studies and the fact that vitamins can be purchased over the counter without prescriptions has increased the vitamin consumption[3,7,8]. Fruits and vegetables are considered as cancer preventing food supplies with their vitamin and nutritional contents[20]. Can et al. have determined that 62.6% of the patients consumed vegetables, 29.1% consumed carrot juice and 33% consumed pomegranate juice[7]. In our study patients consumed fruit and vegetables (100%), carrots (98%), garlic (97%) and pomegranate (93%). It was thought that these fruits were consumed in high amounts because it was known that they contain high amounts of vitamin C.

Cancer cells use sugar 3-5 times more than healthy cells. The only harm of sugar is not that it nurtures cancerous tissue, but excessive consumption of flour and sugar causes weight gain and insulin resistance, and according to some sources their unbalanced consumption is a risk factor in diseases[20,21]. In the study conducted by Can et al. it was shown that 47.5% of the patients consumed bread and pastry and 44.1% consumed honey. In the study conducted by Algıer et al. 19.1% of the patients had started consuming honey[7,17]. In our study, 91% of the patients consumed pastry and milk desserts, 79% consumed honey and 67% consumed black mulberry. In society it is commonly believed that honey and black mulberry are very healthy and this may have led to the increased consumption during the disease.

Proteins are structural units of the body. The protein requirement increases to repair the damaged cells during cancer, chemotherapy, radiotherapy, infections and in the postoperative period. In situations like these higher amounts of protein must be included in the diet. The quality and cooking method of the protein is also important[20,21]. In the study conducted by Can et al. it

was seen that 64.8% of the patients consumed chicken, 60.3% consumed fish and 54.7% consumed milk and dairy products. In our study, 100% of the patients consumed fish, chicken and yoghurt, 92% consumed red meat and 89% consumed milk and dairy products.

Algıer et al. reported that cancer patients had used CAM not to leave any method untried (18.9%), to achieve psychological relaxation (13.5%). Avcı et al. reported that patients used CAM because they believed it would provide benefits (85.2%), others had had benefit (26.2%), it would provided hope for the treatment of their disease (23.5%) and as support for the medical treatment (23.5%)[15,22]. We also had similar findings.

Diseases are not only physical processes and psychosocial factors also play an important part evaluating the patients' quality of life. Aiming to increase the quality of life is the reason most commonly stated for the use of CAM. Some studies demonstrated a positive relationship between CAM use and quality of life, whereas others did not. In one study, the patients using a nutritional approach had higher scores of quality of life[23]. In contradiction, in another study, CAM users had a lower quality of life and poorer social wellness scores[24]. In another study the quality of life scores of patients using CAM did not improve in patients with brain tumours[25]. However, in our study the quality of life scores of patients using CAM was higher. According to these results, it can be concluded that more studies should be carried out to determine the effects of CAM use on the patients' quality of life.

In conclusion CAM use is very common among lung cancer patients in Turkey and it seems that the practice increases the quality of life of the patients.

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Comparison of Decurarization Using Sugammadex and Neostigmine After Rocuronium During Desflurane Anesthesia

Desflurane Anestezisinde Rokuronyum Sonrası Sugammadeks ve Neostigmin ile Dekürarizasyonun Karşılaştırılması

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ABSTRACT

AIM: *We aimed to compare the two drugs, sugammadex and neostigmine, with regard to reversing neuromuscular blockage provided by rocuronium under desflurane anaesthesia.*

METHODS: *In this prospective randomized trial, 80 patients with ASA I-III scores were included. The study included the patients having lower abdominal and urological surgery under general anesthesia. In order to evaluate awakening and extubation differences, the participants were assigned into two study groups S and N. Group S and N included the participants who were given sugammadex and neostigmine, respectively to reverse the neuromuscular blockage created by rocuronium. In both groups extubation was performed when previously clarified clinical criteria were full and after TOF value reached 0.90. Other than TOF value at decurarization moment, minutely TOF values were also recorded for ten minutes after decurarization. The time period between decurarization and extubation was recorded as the extubation time.*

RESULTS: *There was no statistical difference between the demographic data. The extubation time in Group S was significantly shorter. The TOF values of Group S at the 2nd, 3rd, 4th, 5th, 6th, 7th, 8th and 9th minutes were significantly higher than that of Group N.*

CONCLUSION: *In comparison with neostigmine, sugammadex results in faster decurarization and a shorter clinical extubation time following neuromuscular blockage induced by rocuronium administration under desflurane anaesthesia.*

Key words: *desflurane; neostigmine; randomized controlled trial; sugammadex*

ÖZET

AMAÇ: *Desfluran anestezisi altında roküronyum ile sağlanan nöromusküler blokajın düzeltilmesinde nöromusküler blokajın düzeltilmesinde sugammadeks ve neostigmini karşılaştırmayı amaçladık.*

YÖNTEM: *Bu randomize prospektif çalışmada, ASA skoru I-III olan 80 hasta yer aldı. Çalışma alt karın ve ürolojik cerrahi geçiren hastaları içerdi. Uyanma ve ekstubasyon farklılıklarını ortaya koymak için katılımcılar, rokuronyum verilerek sağlanan nöromusküler blokajı kaldırmak için,sugammadeks ve neostigmin verilen S ve N gruplarına ayrıldılar. Her iki grupta da ekstübasyon önceden belirlenmiş klinik kriterler yerine geldiğinde ve TOF 0,90'ı aştığında gerçekleştirildi. Dekürarizasyon sırasında ve sonrasında 10 dakika boyunca dakikalık TOF değerleri kaydedildi. Dekürarizasyon ile ekstübasyon arasında geçen zaman ekstübasyon süresi olarak kaydedildi.*

BULGULAR: *Demografik data açısından anlamlı fark izlenmedi. Grup S'deki ekstübasyon süresi anlamlı olarak kısaydı. Grup S'nin 2, 3, 4, 5, 6, 7, 8 ve 9. dakika değerleri anlamlı olarak Grup N'den yüksekti.*

SONUÇ: *Desfluran anestezisi altında roküronyum ile sağlanan nöromusküler blokaj sonrası neostigmine kıyasla, sugammadeks ile daha hızlı dekürarizasyon ve ekstübasyon zamanı sağlanır.*

Anahtar kelimeler: *desfluran; neostigmin; randomize kontrollü çalışma; sugammadeks*

Introduction

Muscle relaxants are one of the most common used drugs in anaesthesia practice. They are used to facilitate endotracheal intubation, decrease muscle tonus during surgery, and to facilitate controlled ventilation in special cases in intensive care units[1,2]. Although neuromuscular function can reverse itself, fast and total reversal of neuromuscular blockage is necessary in order to avoid residual paralysis and related side effects.

Although acetylcholineesterase inhibitors are used to reverse neuromuscular blockage, a new drug,

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sugammadex, have been used in clinical practice in recent years for this purpose [3]. Sugammadex is the first and only drug to reverse the effects of steroidal muscle relaxants selectively [4].

Our aim in this study is to compare sugammadex and neostigmine with regard to extubation periods, TOF (Train-of-four) values, TOF 0.90 times, and complications, in cases where those drugs are used to reverse neuromuscular blockage generated by the administration of 0.6 mg kg^{-1} rocuronium in patients operated electively under desflurane anesthesia.

Methods

This prospective, randomized study was performed in Şişli Etfal Training and Research Hospital with ASA (American Association of Anesthesia) I-III risk groups between 01/02/2012 and 01/04/2012. The study was approved by the ethical committee, and all participants gave informed consents.

The patients with drug intolerance, renal failure, hepatic failure, neuromuscular junction disease, a history of malignant hyperthermia or who are in ASA IV-V risk groups were excluded from the study.

The study included the patients having lower abdominal and urological surgery under general anesthesia. In order to evaluate awakening and extubation differences, the participants were assigned into two study groups. Group S and N included the participants who were given sugammadex and neostigmine, respectively to reverse the neuromuscular blockage created by rocuronium.

The sample size was calculated with the assumption of a 30% difference between comparison parameters of the groups. Therefore 40 patients were assigned into each group in order to obtain an alpha error of 5% and statistical power of 80%.

A standard dose of 2 mg midazolam was administered intravenously about 30 minutes before the operation for the purpose of premedication. Prior to the operation ECG, mean arterial pressure (MAP), peripheral oxygen saturation (SpO2), heart rate (HR), and postintubation end-tidal carbon dioxide (EtCO2) (Drager Primus, Drager Medical, Drammen, Norway) were all monitorized for each patient. Neuromuscular monitoring was also performed with a TOF device.

TOF device measures muscle twitch strength to project the depth of muscle relaxation during anesthesia. It is a combination of an electrical stimulus generator, transducer, muscle response sensor and a monitor. TOF stimulation is delivered every 15 s (60 mA, 2Hz, pulse duration 0.2 ms). Following each TOF, the monitor automatically calculates and displays the TOF ratio, that is the magnitude of the fourth twitch of the train (T4) as a percentage of the first twitch (T4/T1) × 100.

In this study, for nerve-muscle monitoring, electrodes were placed on the ulnar nerve tract using a TOF device (TOF Watch, Organon Technica, Eppelheim, Germany). Transducers were attached to the thumb and a peripheral heat sensor to the palmar side of the hand. TOF device was calibrated and initial TOF was measured just before the anesthesia induction. Calibration was done by eliciting a number of single twitches: the device automatically sets the response to 100%, and that reference value is stored in memory for the duration of procedure.

A vascular line was obtained using a 16-18 gauge intravenous canulla from the arm free off neuromuscular monitoring. Anesthesia was induced using 5-7 mg kg^{-1} thiopental, 1 μg kg^{-1} fentanyl, and 0.6 mg kg^{-1} rocuronium. Endotracheal intubation was performed 90 seconds after the first dose of rocuronium. Anesthesia was maintained using 5-7% desflurane and a mixture of 50% O2 and 50% medical air.

Once the decrease of the effect of muscle relaxant was measured with the initiation of spontaneous breathing or muscle twitches, 0.2 mg kg^{-1} rocuronium was administered and the time of the last dose was recorded. Desflurane was stopped when the surgeon started to close the skin and 2 mg kg^{-1} sugammadex was administered to the patients in Group S (n=40), while 0.01 mg kg^{-1} atropine and 0.03 mg kg^{-1} neostigmine were administered to the patients in Group N (n=40) for decurarization.

Neostigmine was administered when diaphragmatic movements were seen or when the patient's spontaneous breath effort started clinically at the end of surgery. The neostigmine administration time and the TOF value at this time were recorded by another observer. Extubation was performed when patient was cooperative and followed the commands, could take 50% of normal tidal volume, open eyes, swallow, hold tongue out of mouth and erect the head for at least five seconds, and when the TOF value exceeded 0.90. The time between decurarization and

extubation was recorded as the extubation time. The TOF values were measured minutely for ten minutes after decurarization.

Sugammadex was administered to the patients when the surgical procedure was totally completed. The time of sugammadex administration and the TOF value at this time were recorded by another observer. The extubation criteria were the same for sugammadex group. Extubation time and TOF values for ten minutes after decurarization were also recorded for Group S.

The duration of the operation, the duration of anaesthesia, and the dose of fentanyl used were recorded for both groups. All patients were observed for one hour in the recovery room and any complication including residual curarization was recorded.

Statistics

In addition to the descriptive statistics (mean, standard deviation, median, interquartil range), one way/irreversible variant analysis was used in the repetitive measurements of the multiple groups. For the comparison of the sub-groups, dual groups and of the qualitative data, the Newman–Keuls multiple comparison test, the independent t test and the chi-square test were employed, respectively. Freidman's test was conducted for repetitive measurement of variable groups which are not showing normal distribution; Dunn's multicomparison test for comparison of subgroups; Mann–Whitney U test for comparison of binary groups. Results were considered statistically significant when $p< 0.05$.

Results

There were 20 (50%) female and 20 (50%) male participants in Group S. Group N contained 21 (52.5%) female and 19 (47.5%) male patients. The demographical characteristics and ASA scores were not significantly different between groups (Table 1).

The duration of the operation and anesthesia, dose of fentanyl, total dose of rocuronium, the cessation time of inhalational anesthetics after the last dose of rocuronium, and the time between the last rocuronium dose and decurarization were not different between groups (Table 2). However, the extubation time for Group S was significantly shorter than that of Group N ($p<0.05$) (Table 3).

The TOF values at the 1st and 10th minutes were not different. On the other hand, at the 2nd, 3rd, 4th, 5th, 6th, 7th, 8th and 9th minutes, the TOF values of Group S were significantly higher than those of Group N ($p<0.05$) (Table 4, Figure 1).

We did not observe any complication or side effect in the recovery room.

Table 1. *Demographic characteristics of patients received sugammadex (Group S) or neostigmine (Group N) to reverse the neuromuscular blockage created by rocuronium*

		Group S	Group N	p
Age (year)		41.85±13.88	39.8±11.84	0.479
Gender	Male	20 (50%)	21 (52.5%)	0.823
	Female	20 (50%)	19 (47.5%)	
Weight (kg)		72.05±10.47	73.47±6.9	0.475
ASA group	I	22 (55%)	24 (60%)	0.888
	II	13 (32.5%)	12 (30%)	
	III	5 (12.5%)	4 (10%)	

ASA: American Society of Anesthesiologists

Table 2. *Intra opertaive findings of patients received sugammadex (Group S) or neostigmine (Group N) to reverse the neuromuscular blockage created by rocuronium*

	Group S	Group N	p
Duration of Operation (sec)	5267.5±3223.1	4789.5±3177.13	0.456
Duration of Anesthesia (sec)	6328.75±4473.38	5775.5±3496.42	0.751
Dose of Fentanyl (µcg)	139.75±41.96	135±36.16	0.651

Table 3. *Comparison of sugammadex (Group S) and neostigmine (Group N) after rocurronium to reverse the neuromuscular blockage.*

	Group S	Group N	p
Total dose of rocuronium (mg)	52.37±13.01	53±14.54	0.976
Time between last rocuronium dose and cessation of desflurane (sec)	3006.75±1424.83	2799.75±943.02	0.791
Time between last rocuronium dose and decurarization (sec)	3481.5±1499.32	2859±1093.55	0.076
Extubation time (sec)	130.37±167.29	269.1±135.21	**0.0001***

Tablo 4. *TOF values of the groups given sugammadex (Group S) or neostigmine (Group N) to reverse the neuromuscular blockage created by rocuronium.*

TOF	Group S	Group N	p
1st min	4.9±6.8	8.6±14.39	0.149
2nd min	69.7±30.14	21.32±27.31	**0.0001***
3rd min	106.23±26.23	32.7±34.58	**0.0001***
4th min	107.48±21.38	39.05±32.1	**0.0001***
5th min	122.29±21.76	56.11±38.09	**0.0001***
6th min	131.08±21.46	73.85±46.25	**0.0001***
7th min	118±24.22	79.18±40.14	**0.009***
8th min	116.17±26.36	85.96±34.44	**0.025***
9th min	119.67±24.54	89.07±30.95	**0.025***
10th min	119.67±21.6	106±20.63	0.237

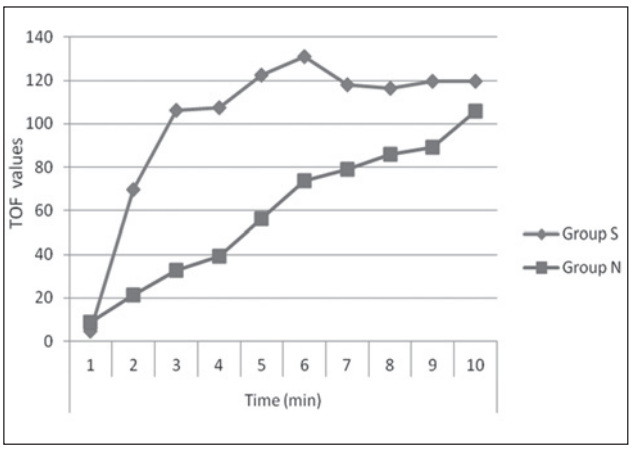

Figure 1. *Time dependent comparison of TOF values of patients given sugammadex (Group S) or neostigmine (Group N) to reverse the neuromuscular blockage created by rocuronium.*

Discussion

Traditionally, acetylcholineesterase inhibitors have been used to reverse the effects of non-polarizing muscle relaxants[3]. However, agents in this group possess potential side effects such as pityalism, and may cause a decrease in cardiac output due to their stimulatory effects on muscarinic and nicotinic receptors. The efficacy of these drugs depends on many factors such as acid-base and electrolyte balance, type of anesthesia, the body weight of the patient, and some antibiotics. In addition, a high dose of neostigmine may cause neuromuscular blockage[4]. It is used together with parasympatholytic drugs like atropine and glycopyrrolate in order to prevent its own side effects. Deep blockage cannot be resolved by neostigmine alone; therefore, it cannot be used in emergencies[5].

Sugammadex is a new pharmacological agent used to reverse the effects of steroidal neuromuscular blockers. It does not have the undesired cholinergic/muscarinic side effects of acetylcholineesterase inhibitors. If given in appropriate doses, it may decrease the duration of effect of rocuronium as of succinylcholine. This property is advantageous in case of difficult intubation or ventilation[6]. It is safer to use succinylcholine which has short-term effect, however combination with sugammadex may cause serious side effects[7]. In appropriate doses, sugammadex reverses neuromuscular blockage, irrespective of anesthetic depth. It does not interfere with the metabolism of acetylcholine, thus it is not necessary to use anticholinergic drugs concomitantly. Furthermore, it has no proven side effects[5,6,8]. Although, there are numerous studies dealing with sugammadex, in our study desflurane was used as the anesthetic agent.

Muscle relaxants during general anesthesia leads to residual effects after surgery in about 20-40% of cases. Residual effects might increase the potential length of hospital stays. Therefore, neuromuscular blockage must be reversed. It is recommended that the TOF value should exceed 0.90 in order to avoid residual blockage and to ensure safe extubation[4,6]. Blobner et al. compared 50 μg kg^{-1} neostigmine and 2 mg kg^{-1} sugammadex under sevoflurane anesthesia and reported that the time needed to attain a TOF value over 0.90 was 18.6 minutes in neostigmine group and 1.5 minutes in sugammadex group[9]. Similarly, in our study TOF value to exceed 0.90 was three and ten minutes in Group S and N, respectively. In addition, there was no residual curarization case in the recovery room.

The recommended dose of sugammadex for immediate reversal of muscle relaxation is between 2 and 16 mg kg^{-1}. Dosage may change according to the depth of the blockage. A dose of 16 mg kg^{-1} is applied in the case of intense neuromuscular blockage, 4 mg kg^{-1} for deep neuromuscular blockage, and 2 mg kg^{-1} for mild neuromuscular blockage[5,8].

The first study on sugammadex administration was performed using a dose of 0.1-8 mg kg^{-1} following a dose of 0.6 mg kg^{-1} rocuronium given to 29 healthy volunteer patients. Muscle relaxation induced by

rocuronium was reversed by using a 4-8 mg kg^{-1} dose of sugammadex within two-three minutes[10]. Makri et al. reported that rebound might be seen in rocuronium effects in the case of sugammadex application below a dose of 1 mg kg^{-1} [11]. It was also reported that after a sugammadex dose of over 2 mg kg^{-1}, blockage ceased in less than three minutes. The reversal time of neuromuscular blockage was about 1.1-1.5 minutes in the case of a 4 mg kg^{-1} use and 1.3-1.7 minutes in the case of a 2 mg kg^{-1} use.

During blockage induced by rocuronium, 2 mg kg^{-1} sugammadex and 50 μg kg^{-1} neostigmine were compared. Sugammadex had a faster reversal effect than neostigmine[5]. In comparative studies, deep neuromuscular blockage performed by rocuronium was compared when 4 mg kg^{-1} sugammadex (2.9 minutes) and 70 μg kg^{-1} neostigmine (50.4 minutes) were used. The blockage was reversed by sugammadex 17 times faster than by neostigmine, and residual block was not seen in any of the patients[3]. In our study, extubation time was recorded in seconds using a chronometer. Extubation took 130.37±167.29 seconds after 2 mg kg^{-1} sugammadex administration. On the other hand, extubation took significantly longer, 269.1±1352.1 seconds, following atropine and neostigmine administration.

In a study performed on morbid obese patients, 35 patients received sugammadex and another 35 patients received neostigmine for decurarization. Mean dose of rocuronium was 87.9 vs 85.6 mg ($P>0.05$), mean time to reach 90% TOF was 2.7 vs 9.6 min ($P<0.05$), and TOF at the post anesthesia care unit was 109.8% vs 85.5% ($P<0.05$), in Groups SUG and NEO, respectively[13]. Likewise, Woo et al., in their study including 118 patients, showed that time for recovery of the TOF ratio to 0.9 was 1.8 (1.6, 2.0) minutes in the sugammadex group and 14.8 (12.4, 17.6) minutes in the neostigmine group ($p < 0.0001$). These results are also similar with our results. Sugammadex was generally well tolerated in these studies, with no evidence of residual or recurrence of neuromuscular blocker (NMB) effect. Four patients in the neostigmine group were reported with adverse events in one study, possibly indicative of inadequate NMB reversal[14]. In the sameway, Wu et al. obtained considerable data in a multicentre study performed on 230 Chinese subjects (sugammadex, n=119, neostigmine, n=111); and 59 Caucasian subjects (sugammadex, n = 29, neostigmine, n = 30). They reported; a geometric mean time (95% CI) for recovery of TOF ratio to 0.9 was 1.6 (1.5–1.7) min with sugammadex vs 9.1 (8.0–10.3) min with neostigmine in Chinese subjects. Corresponding times for Caucasian subjects were 1.4 (1.3–1.5) min and 6.7 (5.5–8.0) min, respectively. Sugammadex 2 mg kg^{-1} was generally well tolerated with no serious adverse events reported. There was no residual NMB or recurrence of NMB effect[15]. Özgün et al. reported that suggammadex was confidently useable for also pediatric patients[16].

In a randomized, controlled study on adult patients, the reverse effects related to sugammadex were lower than 1% in all cases and it was advised that this agent was effective and safe[17]. Only one healthy adult patient showed something similar to a slow, allergic reaction, with flushing and tachycardia, following the administration of sugammadex at a dose of 8.4 mg kg^{-1}. Some other studies reported hypersensitivity and anaphlaxis during sugammadex use[18-21]. In addition, a bitter taste and coughing due to the high dose of the drug were also reported. Moreover, ECG showed QT interval increase in some patients[22].

Neostigmine and sugammadex were again compared in terms of hemodynamic effects in patients having neuromuscular blockage using rocuronium or vecuronium. Although sugammadex group had no heart rate changes, neostigmine had significant heart rate increases[3,12].

Erbaş et al. compared the effects of sugammadex and neostigmine for QT prolongation in rabbits under general anesthesia. Although sugammadex didn't have any influence, neostigmine increased the QT time[23]. Koyuncu et al. reported that extubation, first eye opening and head lift times were shorter in patients given sugammadex. Postoperative heart rates were significantly lower at all times in patients given neostigmine[24]. We did not make a haemodynamic comparison in our study. However, we did not encounter any adverse effects such as bradycardia, tachycardia, hypotension, and hypertension in patients given sugammadex.

In conclusion, in comparison with neostigmine, sugammadex results in faster decurarization and a shorter clinical extubation time following neuromuscular blockage induced by rocuronium administration under desflurane anaesthesia.

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Relation Between Cardiovascular Disease Risk Factors and Common Carotid Artery Intima Media Thickness

Kardiyovasküler Hastalık Risk Faktörleri ve Karotis Arter Intima Media Kalınlığı Arasındaki İlişki

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ABSTRACT

AIM: *To determine the effects of age, sex, smoking, hypertension, diabetes mellitus, hyperlipidemia, history of coronary artery disease and cerebrovascular disease on carotid intima media thickness.*

METHODS: *Patients (N=222) undergoing Color Doppler Ultrasound examination of the extra cranial carotid arteries for any reason in a four-month-period were prospectively investigated. Posterior wall intima media thickness on 1-1.5 cm distal part of both common carotid arteries was measured three times for each patient. The mean values of measurements of right and left common carotid arteries, the presence of atherosclerotic plaque and vessel stenosis ≥ 15% were recorded. The effects of age, sex, smoking, hypertension, diabetes mellitus, hyperlipidemia, coronary artery disease, and cerebrovascular disease on common carotid arteries intima media thickness and the relationship between common carotid arteries intima media thickness and plaque existence were investigated.*

RESULTS: *Age, sex, smoking, hypertension, diabetes mellitus, hyperlipidemia, coronary artery disease and cerebrovascular disease individually increased the common carotid arteries intima media thickness according to univariate analysis. All of the parameters but diabetes mellitus were defined as risk factors by using regression analysis. Hypertension followed by hyperlipidemia, coronary artery disease and cerebrovascular disease had more power.*

CONCLUSION: *Intima media thickness of common carotid arteries is affected by un-modifiable factors such as age and sex and by modifiable factors such as smoking, hypertension, hyperlipidemia, coronary artery disease and cerebrovascular disease.*

Key words: *cardiovascular diseases; carotid intima-media thickness; demography; Doppler; echocardiography; risk*

ÖZET

AMAÇ: *Yaş, cinsiyet, arteriyel hipertansiyon öyküsü, diabetes mellitus, hiperlipidemi, koroner arter ve serebrovasküler hastalık öyküsü ve sigara kullanımının karotis intima media kalınlığı üzerine etkisini belirlemektir.*

YÖNTEM: *Herhangi bir nedenden dolayı kliniğimizde, dört aylık periyotta ekstrakranial karotis arterlere yönelik Renkli Doppler Ultrasonografi incelemesi yapılan olgular (N=222) prospektif olarak değerlendirildi. Her olgunun karotis intima media kalınlığı, her iki ana karotis arterin yaklaşık 1-1,5 cm'lik distal bölümünden, yalnızca posterior duvardan, üçer kez ölçüldü. Sağ ve sol ana karotis arterden ölçülen değerlerin ortalaması alınıp kaydedildi. Aterosklerotik plak varlığı kaydedildi. Çap ölçümüne göre ≥ % 15 darlığı olan olgular seçildi. Yaş, cinsiyet, hipertansiyon, diyabet, hiperlipidemi, kardiyovasküler hastalık öyküsü ve sigara kullanımının ana karotis arterin intima media kalınlığı üzerine etkisi ve plak varlığı ile karotis karotis intima media kalınlığı arasındaki ilişki araştırıldı.*

BULGULAR: *Yaş, cinsiyet, sigara, koroner arter ve serebrovasküler hastalık öyküsü, hiperlipidemi, hipertansiyon ve diabetes mellitus, univariate analizde ana karotis arterin intima media kalınlığı üzerine tek başlarına etkili risk faktörleri oldukları saptandı. Yapılan regresyon analizi sonucunda diabetes mellitus dışındaki tüm parametrelerin ana karotis arterin intima media kalınlığı üzerine anlamlı etkisi olduğu görüldü. En önemli etkinin hipertansiyondan kaynaklandığı bunu, hiperlipidemi, koroner arter ve serebrovasküler hastalık öyküsü değişkenlerinin takip ettiği saptandı. Plak ve darlık saptanan olguların ana karotis arterin intima media kalınlığı ölçümlerinin, saptanmayanlara göre istatistiksel olarak anlamlı düzeyde yüksek olduğu görüldü.*

SONUÇ: *Ana karotis arterin intima media kalınlığı; yaş ve cinsiyet gibi değiştirilemeyen risk faktörlerinin yanı sıra, sigara kullanımı, hipertansiyon, hiperlipidemi, koroner arter ve serebrovasküler hastalık gibi değiştirilebilen risk faktörlerinden etkilenir.*

Anahtar kelimeler: *kardiyovasküler hastalıklar; karotis intima-media kalınlığı; demografi; Doppler; ekokardiyografi; risk*

Introduction

Atherosclerosis is with fatty deposits called atheromatous plaques located on the internal walls of great and moderate arteries. Approximately half of people in the United States of America and in Europe die of diseases related with atherosclerosis[1].

Increased carotid intima media thickness (IMT) is the earliest morphological sign of atherosclerosis and these

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early changes can be easily detected by B-Mode ultrasonography[2,3]. It is stated that there was a relation between myocardial infarction (MI), stroke and coronary artery disease (CAD) related deaths and carotid IMT[4]. The relation between carotid IMT and traditional cardiovascular risk factors such as age, gender, hypertension (HT), diabetes mellitus (DM), hyperlipidemia and smoking in addition to CAD and cerebrovascular disease (CVD) was studied previously[5-19]. However, results of these studies are conflicting.

The present study aimed to determine whether the risk factors such as age, gender, HT, DM, hyperlipidemia, CAD, CVD and active smoking influence carotid IMT.

Methods

The patients undergoing extra cranial carotid artery Color Doppler Ultrasound (CDUS) for various reasons in Lütfü Kırdar Training and Research Hospital Radiology Clinic between May 2012 and August 2012, and between April 2013 and May 2013 were included. All included patients were voluntary to participate and the data were prospectively evaluated. The study was approved by the local ethics committee.

In order to identify the risk factors, the patients were questioned. Age, active smoking habit and history of HT, DM, hyperlipidemia, CAD and CVD were recorded. Exclusion criteria included smokers for less than five years, daily cigarette consumption of less than a half pack, and retrospective smokers quitted.

Patients received antihypertensive therapy or were diagnosed with HT but did not receive any therapy were defined as HT patients. Insulin or oral anti-diabetic drug use or a diagnosis of DM managed with diet therapy was defined as DM. Cholesterol level over 200 mg / dl[1] was considered as hyperlipidemia. History of MI, coronary bypass, angina pectoris and use of drugs for CAD were defined as CAD patients. History of stroke and/or transient ischemic attack (TIA) was considered as CVD. The cases that failed to give adequate anamnesis and the cases that underwent endarterectomy of carotid arteries or that had carotid stent were excluded. A total of 222 cases participated.

Ultrasound (US) examination was performed by an experienced radiologist while the patients were in supine position with the head in mild extension and approximately 20° contralateral cervical rotation. Standard US devices (Logic 9, General Electric Company, USA) and 10 MHz linear transducer were used during examinations.

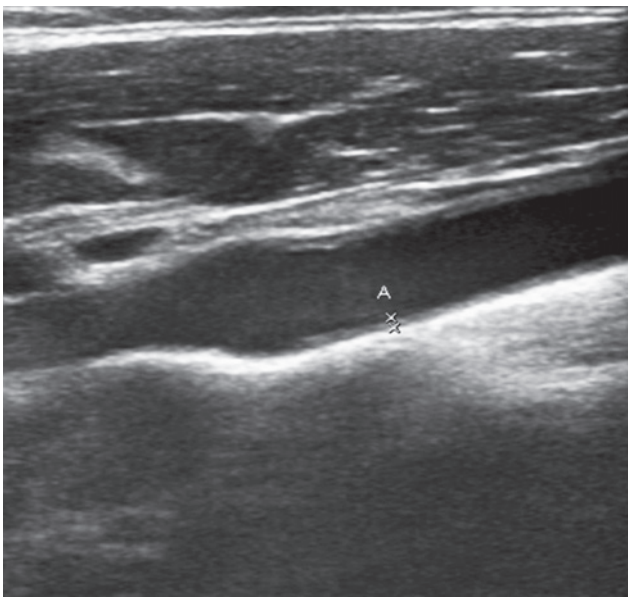

Figure 1. Intima-media thicknesses were measured from the posterior wall at the 1-1.5 cm distal part of Common Carotid Artery.

Common carotid artery (CCA), internal carotid arteries (ICA) and external carotid arteries (ECA) of all cases were evaluated in longitudinal and transverse axes by grey scale, CDUS and Power Doppler Ultrasound (PDUS) techniques. In each case, only posterior wall IMT on the 1-1.5 cm distal part of both CCAs was measured three times (Figure 1). The characteristic echogenicities of lumen-intima media and media-adventitia were used for measuring IMT. The values measured from the right and left CCA were separately recorded and their arithmetical mean was calculated. Segments with atherosclerotic plaque were omitted during measurements. An IMT value of 1.5 mm or higher was considered as plaque[20]. Carotid plaque thickness was evaluated on transverse images (short axis), because it was accepted to demonstrate plaque thickness most correctly[21]. IMT value of 1.5 mm or more on transverse axis was diagnosed and recorded as plaque. The amount of stenosis in the stenotic area was specified proportionally. For this purpose, the NASCET (North American Symptomatic Carotid Endarterectomy Trail) method recommending was used (proportioning narrowest diameter in longitudinal plane to the normal arterial diameter in the distal part)[22]. The cases with a stenosis of ≥15% of the diameter were recorded. Effect of age, gender, HT, DM, hyperlipidemia, CAD, CVD and active smoking on CCA IMT, as well as relation between presence of a plaque and carotid IMT, were investigated.

NCSS (Number Cruncher Statistical System) 2007&PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA) programs were used for statistical analyses. While evaluating study data, in addition to the descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum), for evaluation of quantitative data Student t Test was used as well for paired group comparison of the parameters that showed normal distribution. Relation between the parameters was analyzed by Pearson's correlation analysis. Multivariate Stepwise Linear Regression Analysis was performed to determine the effect of demographic characteristics and risk factors on CCA IMT. The level of significance was evaluated at the levels of $p<0.01$ and $p<0.05$.

Table 1. *Common carotid artery intima media thickness of 222 patients and the distribution of the risk factors*

	Mean±SD	Min-Max
CCA IMT	0.83±0.21	0.30-1.40
	N	%
Plaque	118	53.2
Stenosis	45	20.3
Smoking	69	31.1
CAD	18	8.1
Hyperlipidemia	71	32.0
HT	111	50.0
DM	40	18.0
CVD	25	11.3

CCA: Common carotid artery, IMT: Intima media thickness, CAD: Coronary artery disease, HT: Hypertension, DM: Diabetes Mellitus, CVD: Cerebrovasculary disease.

Results

A total of 222 cases, 152 (68.5%) females and 70 (31.5%) males, participated in the study. The ages of the patients ranged between 15 and 83 years with a mean of 54.31±13.22 years. The reason for being referred to our clinic was vertigo in 149 (67.1%), headache in 22 (9.9%), paresthesia in the upper extremity in 15 (6.7%), tinnitus in 4 (1.8%), syncope in 4 (1.8%), new-onset stroke in 6 (2.7%), and TIA in 2 (0.9%) of the cases. The remaining 20 (9.0%) cases had been referred to our clinic for a regular control visit.

The CCA IMT values of the cases ranged between 0.30 mm and 1.40 mm with a mean of 0.83±0.21 mm. Plaque and stenosis were detected in 53.2% (n=118) and 20.3% (n=45) of the cases, respectively.

The prevalence of smokers was 31.1% (n=69); whereas, 8.1% (n=18) of the cases had CAD, 32.0% (n=71) had hyperlipidemia, 50% (n=111) had HT, 18.0% (n=40) had DM, and 11.3% (n=25) had CVD. Distribution of CCA IMT and the risk factors is demonstrated in Table 1.

Univariate analysis revealed that age, gender, smoking, CAD, hyperlipidemia, HT, DM and CVD were individual risk factors and independently effected CCA IMT. Regression analysis demonstrated that all parameters except DM had significant effect on CCA IMT. It was determined that HT was the most effective factor followed by hyperlipidemia, CVD and CAD. Whilst the effects of CAD and smoking were found to be significant at the level of $p<0.05$, age, male gender, hyperlipidemia, CVD and HT were found to be effective at the level of $p<0.01$. Relation of demographic characteristics and risk factors with CCA IMT is demonstrated in Table 2. The mean CCA IMT increased with

Table 2. *Relation between some demographic characteristics and common carotid artery intima media thickness*

	Extra-Standard coefficients		95.0% Confidence Interval for B	
Model	B	p value	Lower limit	Upper limit
(constant)	0.264	0.001	0.175	0.353
Age	0.007	0.001	0.005	0.008
Gender	0.060	0.004	0.020	0.100
Hyperlipidemia	0.123	0.001	0.086	0.160
Smoking	0.049	0.016	0.009	0.089
CVD	0.082	0.004	0.027	0.136
CAD	-0.068	0.039	-0.132	-0.003
HT	0.137	0.001	0.097	0.177
DM	0.028	0.258	0.026	0.135

CVD: Cerebro vasculary disease, CAD: Coronary artery disease, HT: Hypertension, DM: Diabetes Mellitus,

age (0.007; 95% CI: 0.005-0.008). CCA IMT values were significantly higher in the cases with plaque and/or stenosis ($p<0.01$).

Discussion

Atherosclerosis is a diffuse disease involving various parts of the arterial system[23]. Epidemiological studies indicate many factors contributing to the development and progression of atherosclerosis. In addition to unchangeable risk factors such as genetic susceptibility, local arterial and hemodynamic factors and gender, modifiable risk factors such as HT, hypercholesterolemia, smoking, glucose intolerance, obesity and sedentary life style as well contribute to the development of atherosclerosis[21]. Increased carotid IMT is the earliest morphological sign of atherosclerosis[2]. Typically, atherosclerosis most commonly evolves on posterolateral wall of the bulb and then spreads all around[24].

Histological studies revealed that media and adventitia thicknesses on ultrasound images are quite close to their real thicknesses[25]. Whilst internal hyperechogenic line represents the lumen-intima interface, external hyper-echogenic line represents the media-adventitia interface and the distance between two lines indicates IMT. Thickness increases with age[26]. In addition to the change with age, IMT also increases with earlier plaque formation; therefore, IMT measurement is used as the sign of cardiovascular risk in many clinical settings[27] and the carotid IMT is a strong predictor of cardiovascular events such as MI and stroke. In addition, increased carotid IMT is associated with HT, hyperlipidemia and cardiovascular diseases[28,29]. There are studies suggesting that individuals under risk for atherosclerotic diseases can be determined by measuring carotid IMT in young people and children[30].

Age is among unchangeable factors that contribute to the development and progression of atherosclerosis[21] and the positive correlation between age and carotid atherosclerosis is increasingly being emphasized[6-8]. Consistent with the literature, the present study demonstrated that IMT increased with age.

Atherosclerosis is several times more prevalent in young and middle-aged males versus females. It is suggested that male sex hormones are atherosclerogenic or female sex hormones are protective[1]. The facts that CAD is less prevalent among premenopausal females, symptoms appear meanly 10 years earlier in females versus males and the risk of disease increases with menopausal state confirm this hypothesis[21,31]. As was determined in the present study, the literature comprises the studies that reveal positive correlation between male gender and carotid IMT[7,10,11]. However, there are studies suggesting that gender has no effect on carotid IMT. Ertan et al. stated that gender does not influence carotid IMT and they attributed this to the female participants' being in the postmenopausal state[9].

Smoking is a modifiable risk factor[21,32]. In recent years, combating smoking has become one of the main goals of public health units in the USA and United Kingdom[33]. In the present study, we as well found significant relation between carotid IMT and active smoking. Besides, there are studies in the literature stating that smoking does not influence carotid IMT[7,19]. In their study, Oren et al. stated that smoking does not influence carotid IMT and they related with their sample characteristics consisting of young participants aged 27-30 years[19].

HT is defined as one of the well-known atherosclerotic risk factors[21]. Prospective studies demonstrated that high blood pressure was associated with increased risk of atherosclerotic cardiovascular disease[34,35]. Regression analysis performed in the present study revealed that HT had the most important effect on carotid IMT, as reported previously[7,12,13,36]. However, some studies suggested that HT did not increase carotid IMT[14]. Fabris et al. propounded that HT influenced intracranial arteries rather than extra-cranial arteries[37].

In the present study, we found that carotid IMT was statistically significantly higher in patients with histories of CVD and CAD. Consistent with our study, relation between carotid IMT and hyperlipidemia, CVD and CAD was documented previously[4-6,8,38].

In addition to the researchers in the literature stating that DM increases carotid IMT, there are also researchers reporting no relation[7,15,16,39,40]. In the present study, univariate analyses demonstrated that DM is among the risk factors effective on carotid IMT; whereas, regression analysis revealed no significant effect of DM on carotid IMT. We think this outcome emerges from the fact that substantial proportion of DM participants in the present study consists of individuals with good glycemic control. Studies have put forward that good glycemic control decreased complications of DM. It was emphasized that an increase in HbA1C by 1% provided 14% decrease in MI and 37% decrease in DM-related microvascular complications[41].

Various previous studies have mentioned about the relation between the presence and severity of plaque in carotid arteries and IMT[7,42]. In our study, the carotid IMT was significantly higher in the cases with plaque detected in the extra cranial ICA and CCA. Moreover, we observed that carotid IMT was statistically higher in the cases with a 15% or higher stenosis.

In conclusion, un-modifiable risk factors such as age and gender, as well as modifiable risk factors such as active smoking, HT, hyperlipidemia, CVD and CAD, increase carotid IMT.

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Comparison of Percutaneous Nephrolithotomy Procedures Performed for Simple and Complex Renal Stones

Basit ve Kompleks Böbrek Taşları İçin Yapılan Perkütan Nefrolitotomi İşlemlerinin Karşılaştırılması

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ABSTRACT

AIM: *To compare the percutaneous nephrolithotomy procedures performed for simple and complex kidney stones.*

METHODS: *In this retrospective study, 268 renal stones operated using percutaneous nephrolithotomy, between January 2011 and March 2014, were evaluated. Operations were performed for upper /middle calyx stones and lower calyx stones larger than 2 cm and 1.5 cm, respectively. Success rate, complications, number of percutaneous entry, operation time, and hospital stay were evaluated. The results of the operations of the simple and complex stones were compared.*

RESULTS: *Percutaneous nephrolithotomy was performed in 268 renal units in 186 (73.5%) male and 67 (26.5%) female, with a mean age of 43.1 ± 12.15 (13-78) years. There were 169 (63%) simple and 99 (37%) complex stones. Mean stone burden was 340 mm² (30-760). Mean preparation time for surgery was 27.2 (20-50) min. and mean operation time was 90.4 (40-170) min. Blood transfusion was required in 35 cases. Open surgery was needed in two patients due to perioperative bleeding. Colon injury occurred in one patient.*

Double-J catheter was inserted in 13 patients. Stone clearance rate in simple and complex stones was 78% and 40%, respectively (p<0.01). The rate of success was 87% (n=232) in all patients.

CONCLUSION: *The rate of patients requiring additional treatment and the rate of failure are significantly higher in complex stones than in simple stones. However, percutaneous nephrolithotomy is an effective and safe method providing high success rates, shorter hospital stay, and acceptable complication rates.*

Key words: *complications; kidney; nephrolithotomy; outcome assessment; percutaneous; stone*

ÖZET

AMAÇ: *Basit ve kompleks böbrek taşları için yapılan perkutan nefrolitotomi işlemlerinin bulgularını karşılaştırmak.*

YÖNTEM: *Bu retrospektif çalışmada, Ocak 2011 ve Mart 2014 arasında perkutan nefrolitotomi ile ameliyat edilen 268 böbrek taşı incelendi. Ameliyatlar, iki cm den büyük üst ve orta pol böbrek taşlarına ve 1,5 cm den büyük alt kaliks taşlarına işlem yapıldı. Hastalar başarı oranı, komplikasyonlar, perkütan giriş sayısı, ameliyat süresi, hastanede kalış süresi açısından değerlendirildi. Basit ve kompleks böbrek taşları için yapılan ameliyatların bulguları karşılaştırıldı.*

BULGULAR: *Perkutan nefrolitotomi 186 (%73,5) erkek, 67 (%26,5) kadın hastada, 268 renal üniteye yapıldı. Olguların idi. Yaş ortalaması 43,1±12,15 (13-78) yıldı. Çalışmadaki taşların %63'ü (n: 169) basit, %37'si (n: 99) ise kompleksti. Ortalama taş yükü 340 mm² (30-760) olarak hesaplandı. Cerrahi girişim için ortalama hazırlık süresi 27,2 (20-50) dakika, ortalama operasyon süresi 90,4 (40-170) dakikaydı. Otuz beş olguda kan transfüzyonu yapılırken, iki hastaya ise intra-operatif kanamadan dolayı açık cerrahi yapıldı. Bir hastada kolon yaralanması yaşandı.*

On üç hastaya ise double-J kateter konuldu. Taştan tamamen temizlenme oranı, basit izole taşlarda %78, kompleks taşlarda %40 idi (p< 0.01). Tüm olgular incelendiğinde, % 87'sinin (n: 232) başarıyla sonuçlandığı gözlendi.

SONUÇ: *Kompleks taşı olan hastalarda ek tedavi ihtiyacı ve tedavi başarısızlığı oranı belirgin olarak daha yüksektir. Ancak, yüksek başarı oranı, kısa hastanede kalış süresi ve Kabul edilebilir komplikasyon oranlarıyla, perkutan nefrolitotomi etkin ve güvenli bir yöntemdir.*

Anahtar kelimeler: *komplikasyonlar; böbrek; nefrolitotomi; sonuç değerlendirmesi; perkütan; taş*

Introduction

Percutaneous nephrolithotomy (PCNL) causing lower morbidity and shorter hospital stay has replaced open surgery in the treatment of large kidney stones and has been the method of choice for the treatment of kidney stones larger than 2 cm since 1980[1].

Advances in extracorporeal shock wave lithotripsy (ESWL) and endourology have greatly reduced indications for open surgery[1]. In addition, latest technological advances have increased the success rates of PCNL

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and also the modifications in the procedures of PCNL have significantly reduced morbidity[2,3]. Meta-analyses have reported lower complication rates for PCNL and most of the complications are minor[4].

In this study, we aimed to retrospectively analyze the percutaneous nephrolithotomy applications performed in our clinic and to evaluate them in the light of the current literature.

Methods

This retrospective study included the PCNL applications performed in 268 renal units between January 2011 and March 2014. The study complies with the Helsinki Declaration.

Prior to surgery, whole blood count (WBC), urine analysis and culture, prothrombin time (PT), partial thromboplastin time (PTT), international normalized ratio (INR), and hepatitis indicators (HIV, HBV, and HCV) were evaluated.

Stone surface area was measured as cm^2 by multiplying the longest diameter of the stone by its intersecting vertical diameter using direct urinary system graphy (DUSG). Preoperative evaluations were performed using computed tomography (CT) and intravenous pyelography (IVP). In the patients with positive urine culture, antibiotic therapy was started at least 1 week prior to the procedure.

Based on the results of PCNL, the cases were divided into three groups as (I) 'stone-free', (II) 'clinically insignificant residual fragments (CIRFs)', and (III) 'failed PNCL procedure'. CIRFs were described as non-obstructive and noninfectious stone fragments smaller than 4 mm.

All the patients were operated using cystoscopy under general anesthesia at the lithotomy position. The procedure was initiated by inserting a ureteral catheter (5.0/6.0 Fr open-end ureteral catheter) and the catheter was fixed to the 16/18 Foley catheter which had been previously inserted. Then, the patient was placed in the prone position. At this position, the kidney stones were detected under C-arm fluoroscopy (SireMobil Compact, Siemens, Germany). The anatomy of the renal collecting system was illustrated by retrograde pyelography. The calyxes were entered at a 90° angle using an 18G percutaneous access needle (Microvasive) under multi-planar C-arm fluoroscopy. A guide wire (Sensor guide wire, Microvasive) was inserted through the needle. Dilatation was achieved over the guide wire using filiform dilators and care was taken to advance the guide wire as far back into the ureter as possible. A percutaneous port was created by performing 30F dilatation over the guide wire using Amplatz dilators and a ureteral access sheath was inserted. The stones were fragmented using a 26F rigid nephroscope (Wolf, Germany) and pneumatic lithotriptor (Vibrolith-Elmed, Ankara, Turkey). The fragments were removed through the sheath by using grasping forceps. Following the removal of the fragments, an 18 Fr nephrostomy tube was inserted. The integrity of the system and the insertion of the tube were checked by delivering opaque medium through the nephrostomy tube under fluoroscopy. At the end of the procedure, the ureteral catheter was left as fixed to the Foley catheter.

The nephrostomy tube was removed after clamping for 3-12 h and the ureteral catheter was removed on postoperative day 1. The tube was clamped in the patients presenting with no clinically significant rest stones (>4 mm) on DUSG and with bright urine. In these patients, the clamp was removed after 2-4 h. The tube was removed in the patients detected with no significant residue (>50 cc). A double-J catheter was inserted in the patients with prolonged urinary leakage (>24-48 h). Additional treatments including PCNL, ureterorenoscopy (URS), and extracorporeal shockwave lithotripsy (ESWL) were performed in case where needed. At postoperative third month, all the patients were evaluated using IVP or CT. CIRF stones were accepted as small (<4 mm), asymptomatic, non-obstructive and noninfectious stone fragments, whereas rest stones were accepted as the fragments larger than 4 mm. Successful PCNL outcome was defined as being stone free or having CIRF stones.

Statistical differences and correlations were analyzed using Chi-square test and Spearmen's Correlation Coefficient. A p value of >0.05 was considered significant.

Results

A total of 268 renal units in 253 patients were treated by PCNL. Isolated stones were detected in 238 (94.1%) and bilateral stones were detected in 15 (5.9%) patients. There were 186 (73.5%) male and 67 (26.5%) female patients with a mean age of 43.1 ± 12.15 (13-78) years. Twenty-seven (10.6%) patients had a history of open renal surgery, 47 patients (18.5%) had a history of ESWL at the same side, and 5 (1.9%) patients had solitary kidney.

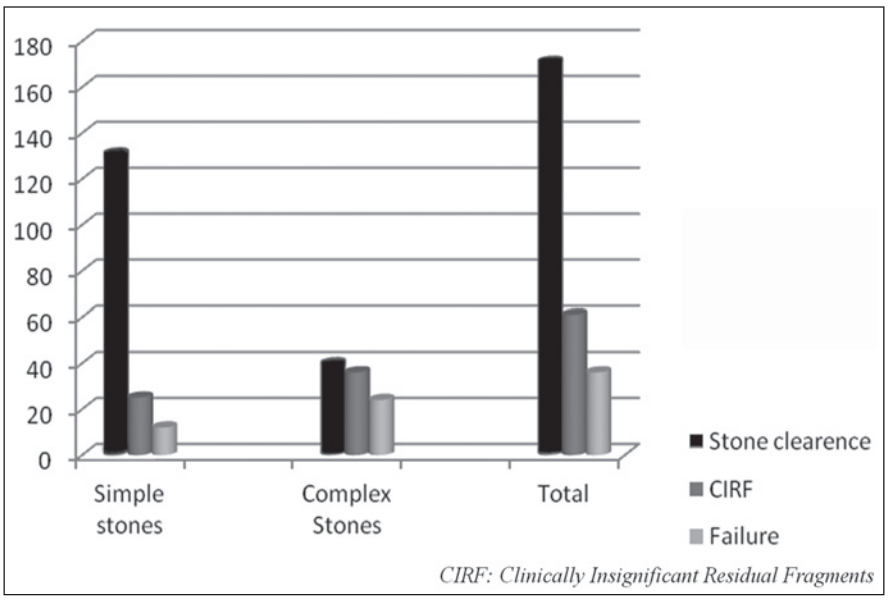

Figure 1. *The success rates for simple and complex stones managed by percutaneous nephrolithotomy.*

The stones comprised 169 (63%) simple stones and 99 (37%) complex stones. Of the simple stones, 80 (30%) were localized in the renal pelvis, 65 (24%) in the lower calyx, and 24 (9%) in the upper calyx. Of the complex stones, 15 (15%) were localized in pelvis and lower calyx, seven (7%) in pelvis and middle calyx, 10 (10%) in pelvis and multi-calyxes, and five (5%) were coraliform stones. Mean stone burden was 340 mm^2 (30-760). Of the 253 patients, subcostal percutaneous entry was performed in 249 (92.9%) and intercostal entry was performed in 19 (7.1%) patients. Single-port percutaneous input was sufficient in 246 patients(92%), whereas a second percutaneous port was required in 22 (8%) patients.

In the follow-up period, 64% (n=171) of the renal units were stone-free, 23% (n=61) had CIRF stones, and PCNL failed in 13% (n=36). One of the patients with failed PCNL had solitary kidney. The additional treatments performed were as follows: Re-PCNL was performed in 11, ESWL in 14, and retrograde intrarenal surgery (RIRS) in eight patients. In three patients, open surgery was performed during the same surgical session due to bleeding (n=2) and failed entry (n=1). Successful outcome was obtained in all of these patients. No nephrectomy was performed in any patient.

Stone clearance rate was significantly higher in isolated simple stones (78% versus 40%) than in complex stones ($p<0.01$). The rate of CIRF was 15% in simple and 35% in complex stones. The rate of patients requiring additional treatment and the rate of failure were significantly higher in complex stones than in simple stones. Figure 1 presents the success rates for simple and complex stones.

Mean preparation time for surgery was 27.2 (20-50) min. and mean operation time was 90.4 (40-170) min. Mean removal time for the nephrostomy tube was 2.7 (range, 1-5) days and mean hospital stay was 3.2 (range, 2-14) days. Following the PCNL procedure, blood transfusion was required in 35 patients. Open surgery was performed in two patients due to perioperative bleeding. Twenty-six patients had postoperative fever (>38°C) and were treated by antibiotic therapy in the follow-up period. Resistant infection was detected in one patient and was treated in 14 days. Colon injury occurred in one patient and was treated by primary treatment. Prolonged urinary leakage was detected in 13 patients 24-48 h after the removal of nephrostomy tube. In these patients, a double-J catheter was inserted and then removed after 3 weeks. Figure 2 presents the complication rates according to stone groups.

Discussion

PCNL is a treatment method providing successful outcomes in transplanted kidneys, complex kidney

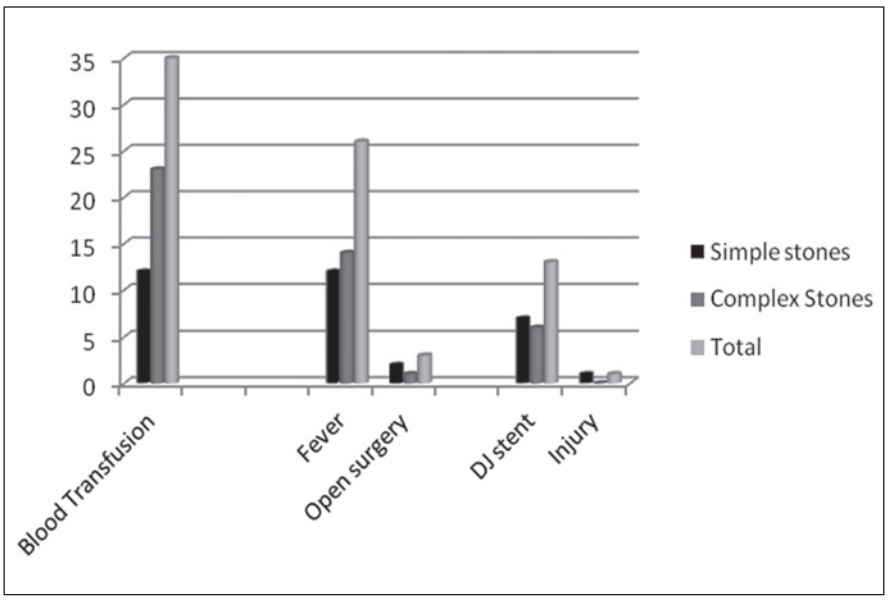

Figure 2. *The complication rates of percutaneous nephrolithotomy procedures performed for renal stones.*

stones, coraliform stones, isolated upper, calyceal, diverticular and ureteral stones. It is also preferred in children, older and overweight patients. Patients with orthopedic deformities and congenital renal anomalies such as horseshoe kidneys and ectopic kidneys are also managed with it[5]. First series of PCNL were reported by Alken and Wickheim in 1981 and the first large-scale studies with more than 1,000 cases were reported in 1985[6]. However, the first large series of PCNL in Turkey was reported in the 2000s[7].

Success rate of PCNL ranges between 40-90% depending on the number and localization of the stones, chemical structure of the stones, and the experience of the surgeon[8]. The success rate of PCNL in Turkey ranges between 60-95% [9,10]. In our study, 64% (n=171) of the renal units were stone-free, 23% (n=61) had CIRF stones, and PCNL failed in 13% (n=36). Therefore, the success rate was calculated as 87%. Stone clearance rate of 78% in isolated simple stones was significantly higher than the rate 40% in complex stones ($p<0.01$). Unquestionably, the rate of stone-free cases is likely to increase as the numbers of cases and the experience of the surgeons increase.

The rate of patients requiring additional treatment following PCNL is reported to be 10%[1]. In our study, the rate of patients requiring additional treatment was 13.4%.

Bleeding is one of the main complications during PCNL. Kessaris et al. reported the rate of bleeding requiring embolization following PCNL as 0.8%[12]. In our study, two patients (<1%) underwent open surgery due to perioperative bleeding. The rate of bleeding requiring blood transfusion during PCNL is reported to be between 14-23%[13,14]. In line with the literature, 13% (n=35) of our patients required perioperative blood transfusion due to bleeding.

Stone size is generally large in complex and coraliform stones. Kukreja et al. reported that stone size had no significant effect on blood loss but it increased the rate of blood transfusion[13]. In our study, the requirement of blood transfusion was significantly higher in patients with complex stones (26%). This situation can be attributed to a number of factors including longer operation times caused by high stone burden, the injury caused by multiple entries, and the entries into the upper pole.

Hydropneumothorax is a common complication reported to occur in 0.7-1.7% of the patients treated by intercostal approach, which is the method of choice particularly for the treatment of upper calyceal stones[9,15]. In our study, no hydropneumothorax was observed and this can be attributed to the limited use of intercostal approach in our patients. Lee et al. reported that pelvic laceration occurred in 0.9%,

ureteral avulsion in 0.2%, and urinoma formation in 0.3% of their patients and the stones slipped into the retroperitoneal space in 1% of their patients[16]. In these series, ureteral avulsion and pelvic laceration were surgically treated, whereas urinoma and stone slippage were treated by conservative therapy. Segura et al. reported that one (0.1%) patient had ureteral laceration and another patient (0.1%) had stone slippage due to ureteral perforation[6]. Also, parenchymal laceration occurred in 2 (0.2%) patients during dilatation and it was treated by open surgery. In our study, no pelvic laceration or ureteral avulsion occurred in any patient. We consider that the rate of these complications is likely to increase as the number of patients treated with PCNL increase. In our series, only prolonged urinary leakage was observed in 13 (4.8%) patients and the patients were treated using double-J catheters. The stents were removed three weeks later and no permanent fistula was observed during the follow-up at three months.

Taşkıran et al. conducted a single-center study with 533 cases and reported that 76.4% of the patients underwent single-port, 16.1% underwent double-port, 7.1% underwent three-port, and one underwent four-port input and no perioperative complication occurred in 92.9% of the patients[17]. In our study, single-port percutaneous input was sufficient in 92% (n=246) and double-port input was formed in 8% (n=22) of the patients. Subcostal percutaneous entry was performed in 92.9% (n=249) and intercostal entry was performed in 7.1% (n=19) of the patients. None of our PCNL procedures was performed using more than two ports. Mean operation time was reported to vary according to the experience of the surgeon. In our study, mean operation time was 90.4 (40-170) min.

Conclusion

The rate of patients requiring additional treatment and the rate of failure are significantly higher in complex stones than in simple stones. However, PCNL is an effective and safe method providing high success rates, shorter hospital stay, and acceptable complication rates.

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Platelet Count and Mean Platelet Volume in the Prediction of Colorectal Cancer in Patients Presented with Emergency Ileus

Trombosit Sayısı ve Ortalama Trombosit Hacminin Acil İleusu Olan Hastalarda Kolorektal Kanseri Öngörmesi

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ABSTRACT

AIM: *We aimed to investigate whether there is a role of platelet number and mean platelet volume in the prediction of colorectal cancer in emergency ileus patients.*

METHODS: *In this retrospective study, ileus cases undergone urgent laparotomy were split into two groups as: Group 1 (G1) included colorectal cancer patients diagnosed with intra operative findings and Group 2 (G2) included patients without cancer. Platelet count and mean platelet volume values were compared between two groups.*

RESULTS: *Distribution of female/male patients between groups were homogeneus (p: 0.724), however mean age of colorectal cancer cases were higher (p: 0.008). Mean platelet volume values and platelet count were higher in cases with colorectal cancer (p: 0.040 and p: 0.004, respectively). Mean platelet volume had 63.3 % sensitivity and 56.5 % specifity, and platelet count had 63.3 % sensitivity and 62.9 % specifity in prediction of colorectal cancer amongst emergency ileus cases.*

CONCLUSION: *Higher platelet count and mean platelet volume values may predict colorectal cancer in cases with acute abdomen diagnosed with ileus.*

Key words: *colorectal cancer; ileus; mean platelet volume; platelet*

ÖZET

AMAÇ: *Trombosit sayısı ve ortalama trombosit hacminin acil ileus endikasyonu ile ameliyat edilen hastalarda kolorektal kanseri öngörmede rolü olup olmadığını araştırmayı amaçladık.*

YÖNTEM: *Bu retrospektif çalışmada, ileus tanısıyla acil laparotomi yapılan hastalar iki gruba ayrıldı: Grup 1 (G1) intraoperatif bulgulara göre kolorektal kanser tanısı alanlar ve Grup 2 (G2) kanseri olmayan hastalar. Trombosit sayısı ve ortalama trombosit hacmi iki grup arasında karşılaştırıldı.*

BULGULAR: *Gruplar arası kadın/erkek dağılımı homojendi (p: 0,724), ancak kolorektal kanser saptanan hastalardaki yaş ortalaması daha yüksek idi (p: 0,008). Kolorektal kanser saptanan hastalardaki ortalama trombosit hacmi ve trombosit sayısı anlamlı düzeyde yüksekti (sırasıyla, p: 0,040 ve p: 0,004). Kolorektal kanseri öngörmede; ortalama trombosit hacmi %63,3 sensitivite, %56,5 spesifite ve trombosit sayısı %63,3 sensitivitesi ve %62,9 spesifiteye sahipti.*

SONUÇ: *Akut abdomeni olan ve ileus tanısı konulan olgularda, daha yüksek trombosit sayısı ve ortalama trombosit hacmi kolorektal kanseri öngörebilir.*

Anahtar kelimeler: *kolorektal kanser; ileus, ortalama trombosit hacmi; platelet*

Introduction

Ileus is complete or partial obstruction of intestinal content's distal transition and develops depending on mechanic or paralytic reasons in intestinal peristalsis. Approximately 80% of ileus develops in small intestine and its frequency increases in middle aged and elderly patient population[1].

Etiological factors have a direct dependency on the age of the patient. While congenital abnormalities are most dominant reasons in newborn infants and children, adhesions in adults, and adhesions and malignancy in geriatric population take place on the top[2]. Management

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varies from conventional medical therapy to massive intestine resections.

Thrombocytes (platelets) are blood cells playing the primary role in homeostasis and coagulation. They are small, coreless, ovoid or round cells. Blood concentration is between 150,000 and 400,000/L. Their half life is 8-12 days.

Thrombocyte volume and increase in its size as well as its number are used in evaluation of inflammatory response in body. In different studies conducted, while it is denoted that platelet volume increases in such cases as acute coronary syndrome, diabetes mellitus, cerebrovascular accidents, hypercholesterolemia, increase in intra abdominal pressure, sepsis and malignancy[3-8].

In this study, we aimed to investigate whether there is a role of platelet number and mean platelet volume in the prediction of colorectal cancer in emergency ileus patients.

Methods

In this retrospective study, the records of 105 patients admitted to emergency service between the dates of January 2013 and October 2014 were evaluated. In accordance with Helsinki Declaration criteria, in pursuit of receiving local ethics committee approval we started the study.

The study included the patients with the complaints of abdominal pain, nausea, vomiting and inability to defecate and operated under emergency conditions with the diagnosis of ileus. The diagnosis was dependent on physical examination, laboratory and imaging findings.

Age, gender, platelet number, mean platelet volume (MPV), intra operative findings, surgical procedures and postoperative histo-pathological examinations were analyzed.

Thirteen patients with incomplete and missing records, accessional malignancy, active infection history and blood products transfusion history in the last fifteen days were excluded.

Patients were split into two groups as: Group 1 (G1) included colorectal cancer patients diagnosed with intra operative findings and Group 2 (G2) included patients without cancer. Dependent variables of age, gender, platelet number, mean platelet volume were compared between groups. Reference value for MPV was taken as 7-11 fL and it was taken as 150-400x10^9/L for platelet number. Hematological parameters were studied in ® LH 780 Analyzer device (Beckman Coulter Inc. Brea, USA).

Statistical Analysis

The data was analyzed using SPSS for Windows 17 (Chicago, İL, USA) packaged software. Distribution of continuous variables was tested by Kolmogorov-Smirnov test. Descriptive statistics were denoted as mean±standard deviation or median (minimum-maximum) for continuous variables, but categorical variables were pointed out as case number and in the form of percentage (%). While the significance of the difference between groups in terms of averages was analyzed via student's t-test, it was analyzed via Mann Whitney U test in terms of median values. Categorical variables were evaluated with the help of Pearson chi-squared test or Fisher's exact chi-square test. The commutual effect of independent variables was detected through cox regression analysis. Roc curve analysis was conducted to calculate the sensitivity, specifity of MPV value and also positive and negative predictive values. For $p<0.05$, the results were accepted as statistically significant.

Results

A total of 92 patients' records were suitable for analysis. The median value for the age was 59 (min: 18- max: 81) and female/male ratio is 0.56. All the operations were performed under emergency conditions. Of the 92 patients 30 (32.6%) were diagnosed with colorectal cancer, and 62 were cancer free.

Co-morbid factors including hypertension (HT), diabetes mellitus (DM), coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD) and heart failure (HF), history of a previous laparotomy, and the gender distribution of the patients was summarized in Table 1.

The mean age was significantly higher in G1 in comparison with G2 (65.3±11.2 and 54.4±17.3, p: 0.008). MPV values of 8.64±0.88 fL in G1 were significantly higher than the MPV values of 8.22±0.70 fL in G2 (p: 0.04). Similarly, platelet number was significantly higher in G1 in comparison with G2 (336400±102600/mm^3 versus 271300±89200/mm^3; p: 0.004).

Co-morbid factors such as DM, COPD and CAD effect MPV levels[9,10]. Thus, we performed cox regression analysis to identify the effects of co-morbid factors.

Table 1. *Demographics of the patients included in the study. The data was present as mean ± SD, median or percentage (N=92).*

Age		58.0±16.4
Gender (Female/Male)		33/59
Colorectal cancer ratio		30 (32.6%)
Co-morbid factors	Non-comorbid factors	33 (35.9%)
	Laparotomy history	41 (44.6%)
	DM,HT,CAD,COPD,CHF	18 (19.5%)
Performed operation	Bridectomy	51 (55.4%)
	Left hemicolectomy based on left colon tumor	12 (13.0%)
	Ostomy based on inoperable colorectal cancer	11 (12.0%)
	Right hemicolectomy based on right colon tumor	5 (5.4%)
	Bezoar ileus	3 (3.3%)
	Small intestinal resection based on Crohn's disease	5 (5.4%)
	Small intestinal resection based on strangulated hernia	2 (2.2%)
	LAR/APR based on rectal tumor	2 (2.2%)
	Left hemicolectomy based on volvulus	1 (1.1%)

HT: Hypertension, DM: Diabetes mellitus, CAD: Coronary artery disease, COPD: Chronic obstructive pulmonary disease, CHF: Congestive heart failure, LAR: Low anterior resection, APR: Abdomino perineal resection

The analysis resulted that MPV level and platelet number might predict ileus development in colorectal malignancy in case where effect of age, gender and co-morbid factors were neglected (p: 0.004 and p<0.001, respectively). Roc curve analysis showed a cut-off value of 8.45 fL of MPV had a sensitivity of 63.3% and a specifity of 56.5% to predict colorectal cancer in patients with ileus (Figure 1). Similarly, a platelet count cut-off value of 289000/mm^3, had a sensitivity of 63.3% and a specifity of 62.9% to predict colorectal cancer in patients with ileus (Figure 2).

Discussion

In our study we identified the MPV and platelet count as useful markers to predict colorectal in cancers in patients undergoing emergency laparotomy with the diagnosis of ileus. However, our study was retrospective and the sample size was relatively small.

Since 1980s, platelet number and platelet volume parameters have been demonstrated together in automatic complete blood count profile without bringing extra costs[11]. The platelet parameters are markers accessed easily, without incremental cost need, stable in female-male and not effected by menstrual cycle for females[11-13]. Thus, as markers MPV and platelet count may be studied in primary care units without difficulty.

Ileus occurs in small and large intestines in 80% and 20% of the cases, respectively. However, malignancies mostly present with colonic ileus (65%), while adhesions presenting with small intestinal obstruction (60%)[14]. The most frequent surgical procedure ascertained in our study is bridectomy connected with adhesions which has coincided with literature and the gender distribution in ileus is roughly equal[15].

Blood platelets have a part in many inflammatory events in body. In malignant cases, an increase is seen in platelet numbers with two different mechanisms. The first mechanism is dependent on interleukin-6 (IL-6) by tumor cell and vascular endothelial growth factor stimulus (VEGF) and megacaryocyte activation in bone marrow, whereas the second one is directly dependent on the thrombocytosis of tumor cell[16-18].

In a study where Karagöz et al. and Pedersen et al. searched platelet number in cases with lung cancer, they stated that platelet number in malignant cases was higher than those in healthy individuals[8-19]. In a research where Jun et al. searched platelet parameters in middle age cancerous cases, MPV, platelet distribution

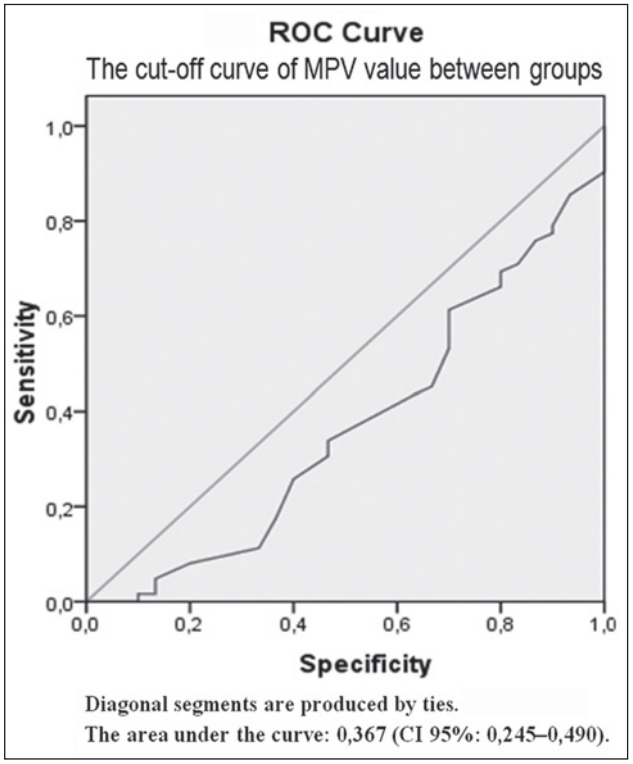

Figure 1. *ROC curve of mean platelated volume assesment to predict colo-rectal cancers in patients presented with emergency ileus.*

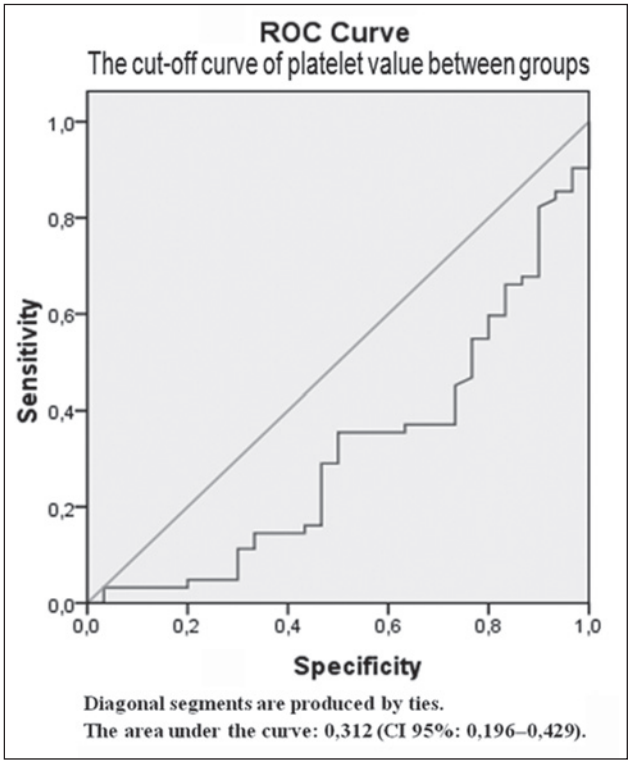

Figure 2. *ROC curve of thrombcyte count assesment to predict colo-rectal cancers in patients presented with emergency ileus.*

wideness (PDW) and platelet size were significantly higher in malignant group than healthy group[20]. Ma et al. detected significantly higher levels of platelet counts in high-grade tumors. In addition, platelet number, MPV and PDW was detected higher in malignant group[21]. In harmony with literature, it was identified in our study that both platelet number and MPV level had been significantly higher in the group where colorectal malignancy was detected among the patients operated under emergency conditions with the diagnosis of ileus.

In ileus, shortly the obstruction of intestinal content's distal transition, lots of factors such as hypokalaemia, adhesions, neurological diseases, abdominal hernia, malignancies and intestinal rotation abnormalities may play a role in pathogenesis. Many underlying etiologic factors may cause differences in the sequence of occurrence of the symptoms. Obstruction degree, type and level vary. However, nearly all patients have complaints such as bloating, nausea, vomiting, inability and abdominal pain. In addition, most of the health care centers lack advanced tools. Moreover, it is still difficult to diagnose intestine obstruction under emergency conditions in spite of up-to-date diagnostic and therapeutic modalities. In Turkey, diagnosis-confirmatory urgent endoscopy and tomography service are not available in many centers. Therefore, clinicians seek simple predictive markers to transfer urgent operation indications from pre-diagnosis of ileus-induced acute abdomen to pre-diagnosis of tumor ileus-induced acute abdomen, which is one step further than the former one. Based on this necessity, it has been made out that platelet number and volume analyzed in te study may predict the detection of colon and rectal cancers.

We consider that the increases in platelet number and MPV level measured automatically via routine hemogram test without bringing any extra costs may predict colorectal carcinogenesis at acceptable rates in patients operated under emergency conditions with the diagnosis of ileus-induced acute abdomen. However, the findings of our study should be confirmed with prospective studies including a larger sample size.

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Prognosis of Clinically Insignificant Residual Renal Stone Fragments Following Therapy with Minimally Invasive Techniques

Minimal İnvaziv Tekniklerle Tedavi Sonrası Klinik Önemsiz Rezidü Böbrek Taşı Parçalarının Akıbeti

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ABSTRACT

Following the treatment with minimally invasive surgical techniques, residual renal stone fragments may make a negative impact on the life quality of patients by causing symptoms. The term of clinically insignificant residual stone fragments is used to describe the asymptomatic and non-obstructive posttreatment residual fragments remained in the kidney, which are smaller than 4 mm (or 5 mm), and associated with sterile urine. However, the stone fragments may cause the formation of a new stone acting as a nidus. The accumulated evidence suggests that there is no significant difference between treatment and follow up in short term, however the stone disease recurs in 20% of the cases in long term. Thus, close follow-up of the patients with clinically insignificant residual fragments is mandotary. Lifestyle changes and medical therapy may be helpful in the management and prevention of new stone formation.

Key words: *kidney stones; lithotripsy; review; ureteroscopic surgery*

ÖZET

Minimal invaziv cerrahi teknikler ile tedavi sonrasında kalan rezidü böbrek taşı parçaları, belirtilere neden olarak hastaların hayat kalitesi üzerine olumsuz etki yapabilirler. Klinik önemsiz rezidü terimi, tedavi sonrasında böbrekte kalan, 4 mm (bazen 5 mm) ve daha küçük olan, asemptomatik, obstrüksiyona neden olmayan ve idrarın steril olduğu durumdaki taş parçaları için kullanılır. Bununla birlikte, klinik önemsiz rezidü için önemli bir nokta da nidus şeklinde yeni taş oluşumuna neden olabilmesidir. Biriken veriler kısa dönemde tedavi etmekle, takip arasında fark olmadığını söylese de, uzun dönemde %20 olguda yeni taş hastalığı gelişir. Bunun için klinik önemsiz rezidü taşı olan hastalarda yakın takip zorunludur. Yaşam tarzı değişikliği ve medikal tedavi sağaltım ve yeni taş oluşumunun önlenmesinde yardımcı olabilir.

Anahtar kelimeler: *böbrek taşları; lithotripsi; derleme; üreteroskopik cerrahi*

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Introduction

Symptomatic urinary stones failing to pass spontaneosly are managed with various treatment options. Appropriate individual treatment choice depends on various facts. Stone burden, localization, size and type of stone, presence of urinary tract infection or congenital anatomical abnormalities may be effective. Extracorporeal shock wave lithotripsy (ESWL), ureterorenoscopy (URS), retrograde intrarenal surgery (RIRS), percutaneous nephrolithotomy (PCNL), laparoscopic and open surgeries may be options.

The residual stone fragments after open surgical procedures were accepted as failure or insufficient treatment. Although open surgical procedures have been replaced by minimally invasive surgical techniques by many surgeons, stone remnants may persist in the urinary system and the remained stone fragments after minimally invasive surgery stone are not cleared immediately. Thus, the term of clinically insignificant residual fragments (CIRFs) is used to describe such posttreatment residual fragments, which are smaller than 4 mm (or 5 mm), asymptomatic, non-obstructive and associated with sterile urine.[1,2] The residual stone fragments may interfere with the quality of life of patients and the residual fragments can lead to stone formation acting as a nidus.

Definition and Outcomes of Clinically Insignificant Residual Fragments

The success of an open stone surgery was defined as removing all of the stones. Remained stone fragments

were accepred as the failure of the treatment. However, current treatment modalities changed the treatment goals. With minimally invasive procedures, the success of the intervention depended on the the size of the remaining stone fragments and fragmentation rates. Thus, stone fragments smaller than 4 mm in size were defined as "clinically insignificant".

Regrowth of the residual stones has been detected with higher incidences after ESWL and minimally invasive procedures[3-5]. Residual fragments following ESWL or PNL lead to high rates of symptomatic episodes, as well as high rates of repeat intervention[6]. The incidence and/or rates of recurrent disease vary with the type of stone, size of the fragment and the type of the procedure.

CIRFs after Shock Wave Lithotripsy (SWL)

Streem and co-workers determined the clinical significance of small, asymptomatic, non-infectious stone fragments after SWL.[7] The authors followed up 160 patients for a mean period of 23 months. Asymptomatic patients with 4 mm or smaller calcium oxalate and calcium phosphate stone fragments after SWL were included in the study. Stone-free status or a decreased, stable or increased amount of residual stone occurred in 38 (23.8%), 26 (16.3%), 67 (41.9%) and 29 (18.1%) of the 160 patients, respectively. The probability of a stone-free, stone-free or decreased status, or stone-free decreased or stable status was 0.36, 0.53, and 0.80, respectively at fifth year after SWL. Ninety one patients (56.9%) were asymptomatic while 69 (43.1%) were symptomatic or required intervention during a mean period of 26 months (1.6–85.4 months) after SWL (probability estimated at 0.71 at 5 years). The authors stated that patients with small non-infectious stone fragments could be followed expectantly after SWL, however a significant number of patients had symptomatic episodes or would require intervention within two years. They concluded that the application of the term CIRFs after SWL might not be appropriate.

Zanetti and co-workers reviewed the therapeutic implications and long-term outcome of asymptomatic patients with dust and residual fragments (less than 4 mm) at third month after SWL[3]. A total of 129 patients were re-examined with radiographic studies, renal ultrasonography and urine culture at 12th month, and 95 were also evaluated at 24th month. The patients were defined as stone-free or with persistent lithiasis or with regrowth stone. At the end of the 12-months follow up period, 60 patients (46.5%) were stone-free and 56 (43.5%) still had residual fragments or dust. There was no significant difference between the stone free rates, size and localization of the stones or fragments at three months and 12 months; however stones or fragments larger than 10 mm enlarged more frequently (11 of 40 patients, 27.5%, versus 2 of 89, 2.2%; P ¼ 0.001) in 13 patients (10%). The probability of eliminating residual lithiasis at 12th month was significantly higher in patients with dust than in those with residual fragments (42 of 79 patients, 58%, versus 18 of 50, 36%; P=0.026). They concluded that in short term follow up period, the patients with fragments do not require systematic retreatment; however if symptoms persisted or stones recurred they might be followed and retreated in long-term.

Buchholz et al. investigated the fate of residual fragments, less than 5 mm, after SWL over a long period.[8] The study aimed to determine the rate and time of the sponteneous pass of the fragments. They also aimed to clarify regrowth, recurrence and their role in clinical outcome. The records of 266 patients containing a mean follow up period of 387 days were analyzed. Fifty five patients (21%) with residual fragments <5 mm in diameter were detected after SWL. Sex, age, medical history, and SWL retreatment rates were not significantly different between the patients with or without residual fragments. After a mean follow up period of 2.5 years, 12.7% of the patients with residual stones had not passed the fragments spontaneously, but all of them were in clinically stable status and the fragments were located in the proximal ureter and the lower calices. Stone regrowth was observed in only 2% of the patients with residual fragments and no stone recurrences were observed within the follow-up period. The authors concluded that more invasive procedures to reach stone free status were not essential.

In a study by Khaitan et al. 81 patients were followed after SWL to clarify the fate of the CIRFs for a mean period of 15 months (6–60 months). In 18 patients, the fragments passed spontaneously during the follow-up, 13 patients were in clinically stable status, and 44 patients develeoped cninically significant complications. Thus, percutaneous nephrolithotomy in three, ureteroscopic stone removal in four and repeat SWL in 16 patients were needed. Conservative analgesic treatment was sufficent in the remaining 21 patients. CIRFs in the caliceal location mostly became symptomatic and 53% of the CIRFs located in the pelvis passed

spontaneously. In addition clinical symprtoms were related with the stone burden and number of stone fragments. Moreover, the clearance rate was highest during the first six months. Finally, the rate of complications correlated with the duration of follow up, the number and size of residual fragments. The authors stated that patients with residual stones required close follow up and timely adjuvant therapy after SWL. For spontaneous passage, the pelvic location was a favorable factor. Although the clearance rate of CIRFs with repeated SWL was lower than the operative techniques, most patients improved with this modality.[9]

Rassweiler and co-workers, in their review analyzed the data obtained from 14000 patients.[2] They compared the data with long-term results of two centers in Germany by comparing the stone localization, stone size, observation time and the anatomical kidney situation. They found that the stone passage was continuous during a 24 months follow up period after SWL. New generation equipments and technology in SWL have increased the CIRFs percentage. The authors stated that 25%, 55% and 20% patients with CIRFs would be stone-free or remain clinically insignificant or clinically significant, respectively, during follow up. If there was not any clinical symptom, secondary interventions would be considered as over-treatment. Only 4–25% of their patients required an additional intervention which was mostly a repeat SWL.

CIRFs after Ureteroscopy

Rebuck et al. investigated the fate of postureteroscopic renal stone fragments less than 4 mm[10]. The aim of ureteroscopy is to fragment stones, and remove larger fragments with basket catheter and allow the small pieces to pass spontaneously. From May 2001 to July 2008, patients treated with ureteroscopy and holmium laser lithotripsy by a single surgeon were included in the study. Fifty one of 330 ureteroscopies met inclusion criteria. Patients with residual renal fragments measuring 4 mm on initial postoperative CT and at least one additional follow up CT were included. Spontaneous passage of the fragments, regrowth of the fragments, and stone events like emergency visits, hospitalization and additional interventions were recorded. The mean follow-up duration was 18.9 months (1.6 years). During follow up, among 46 patients, nine (19.6%) experienced a stone event, 10 (21.7%) passed their fragments spontaneously, and the remaining 27 (58.7%) were in clinically stable status and asymptomatic. The mean fragment size was similar as 2.7, 3.3, 3.5, and 3.0 mm at mean follow-up durations of 2.8, 10.2, 16.8, and 33.0 months, respectively. The authors concluded that approximately one in five (or 19.6%) of the patients with postureteroscopic CIRFs would experience a stone event over the following 1.6 years. The remaining patients will either became stone-free via spontaneous passage or retained asymptomatic stable-sized fragments.

CIRFs after Percutaneous Nephrolithotomy (PCNL)

Altunrende and associates analyzed the data of 430 patients who underwent PCNL during a three-year period and defined CIRFs as asymptomatic, noninfectious stone fragments less than 4 mm[11]. Stone-free rate for their study was 74.5%, and CIRFs were detected in 22% of cases by kidney-ureter-bladder (KUB) graphy three months after surgery. Thirty eight patients with CIRFs after PCNL were included in the study for a mean period of 28.4±5.3 months follow-up and 26.3% of patients had a stone event that needed medical treatment during follow-up, while others were asymptomatic. An increase in the size of the fragments was detected by radiologic assessment in 21.1% of patients, while the sizes were stable or decreased in 71.1% of cases. Three (7.9%) patients had passed their stones spontaneously. Metabolic evaluation revealed metabolic abnormalities in 10 (26.3%) patients. Magnesium ammonium phosphate (struvite) was detected by stone analysis in three of eight patients with increased sizes of residual fragments. In addition, only one of these eight patients had hypocitraturia and one of eight had hypercalciuria as a metabolic abnormality. They concluded that CIRFs after PCNL had progression in medium-term follow-up (most common in first two years). Increase in fragment size was common in patients with struvite stones, and presence of risk factors in 24-hour urine metabolic analysis did not seem to predict growth.

Ganpule and Desai analyzed the outcomes of residual fragments after PCNL and they aimed to determine the factors predicting spontaneous passage[12]. The authors analyzed the outcomes of 2469 patients after PCNL between January 2000 to January 2008. Residual stone fragments were detected in 187 (7.57%) patients. The mean size of fragments was 38.6 ± 52 mm^2 and the most common localization of the fragments was lower calyx (57.7%). Eighty-four patients (approximately half of the patients) passed their stones spontaneously at a mean follow-up period of 24 months. 65.4% of

these stones passed in three months. Size of the fragments were less than 25 mm^2 and pelvic location had the best chance of clearance. The authors stated that surgeon experience, size of residue, presentation time of residue, presence of double-j stent, preoperative nephrostomy drainage, a history of intervention, metabolic abnormalities such as hypercalcuria and hyperuraecemia were significant in predicting the fate of residuel fragments after PCNL.

CIRFs in Children

The definition is adapted from adult studies, thus the fate of CIRFs is not known well in children. Afshar et al. studied residual stone fragments (5 mm or less) following SWL in children. The records of 83 patients (39 boys and 44 girls) and 88 renal units with urinary stone disease after SWL were analyzed. The median age, average stone burden and follow up period were 7 years, 14 mm and 46 months, respectively. Forty renal units (46%) became stone-free after first session of SWL and 18 renal units (20%) had residual fragments. Twelve of the remaining 30 (34%) units rendered stone free after additional interventions including SWL and surgical procedures. Residual fragments were detected in remaining eight renal units. A total of 26 renal units with residual fragments were included in the study. Regrowth of residual fragments, calculi recurrence in stone-free cases and symptomatic episodes were recorded. Eighteen renal units (69%) had residual fragments growth or symptoms, and eight (31%) patients had no stone growth or symptoms. The growth of residual fragments was associated with metabolic disorder presence (odds ratio 11.4). The authors concluded that residual fragments after SWL increased the chance of adverse clinical outcome and these fragments were clinically significant in children. Patients with residual fragments, especially those with metabolic disorders, required close follow up[13].

Dincel et al. assessed CIRFs in children after SWL, PCNL and retrograde intrarenal surgery (RIRS). Eighty five children were followed up for a mean period of 22 months. Spontaneous passage of the fragments, regrowth of the fragments, and stone events like emergency visits, hospitalization and additional interventions were recorded. Only 22 children (25.8%) had passsed the residual fragments spontaneously. Thirty four patients had (40%) renal colic, heamaturia or urinary tract infection, and 20 (23.5%) patients required medical treatment. Regrowth of the residual fragments were detected in 18 children (21.2%) and secondary intervention was required in 25 children (29.4%). They concluded that, the term of CIRFs was not appropriate for postoperative residual fragments in children[14].

Management of Residual Stones

The possible complications of residual stones are related to dislocation of fragments with obstruction and symptoms, persistent urinary tract infection and the risk of develeoping new stones from the nidus[5,15-18].

Patients with residual fragments require close follow-up to monitor the course of stone disease. Adjunctive treatment with tamsulosin may improve the clearance and the stone-free rate after SWL and ureterorenoscopy[19]. Treatment includes high diuresis and mechanical percussion for small fragments located in tle lower calix to facilitate the stone clearence[20]. A diet containing high intake of fluids, vegetables and fruits; lower consumption of protein and salt and a balanced intake of fats, calcium and carbohydrates constitutes an efficacious tratment and prevention approach.

Regular exercise, appropriate body weight, and reducing stress are also useful preventive actions.[21] To prevent the complications, identification of biochemical risk factors is particularly indicated in patients with residual fragments or stones[19]. Since the metabolic disturbances underlying stone formation persist after procedures, recurrence of the disease is inextricably linked to the institution of medical therapy (eg, thiazide diuretic and low salt diet for hypercalciuria, and potassium citrate for hypocitraturia, allopurinol or potassium citrate for hyperuricosuria). It was shown that medical therapy is effective in preventing stone growth and recurrence[22].

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Giant Submandibular Gland Duct Sialolith: A Case Report

Dev Submandibuler Gland Kanal Taşı: Bir Olgu Sunumu

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ABSTRACT

Sialolithiasis is one of the most common diseases of the salivary glands and is characterized by the obstruction of salivary gland or its duct due to the formation of calcareous plaque. The term of giant sialolith is used for the stones over 15 millimeters or 1 gram. It is rarely reported in the literature. We reported a case of a sialolith measured between 25 to 30 mm and located in the submandibuler gland orifice. We excised the sialolith via intraoral approach. Normal saliva flow must be performed during treatment. Minimal invasive surgery is recommended.

Key words: *sialolithiasis; salivary gland diseases; submandibular gland*

ÖZET

Siyalolitiazis, tükrük bezlerinin en sık karşılaşılan hastalıklarından biridir. Siyalolitiazis, tükürük bezinin veya kanalının kalkareoz plak oluşumuna bağlı tıkanmasıyla karakterizedir. Dev sialolit tanımı 15 milimetreden büyük veya 1 gramdan ağır taşlar için kullanılmaktadır. Literatürde nadiren bildirilmiştir. Bu yazıda, boyutu 25 ile 30 milimetre arasında olan bir dev sialolit olgusu sunduk. Bizim olgumuzda sialolit submandibuler gland orifisinin girişine yerleşmişti. Sialoliti intraoral yaklaşımla eksize ettik. Tedavide normal tükürük akışı sağlanmalıdır. Cerrahi olarak minimal invaziv yaklaşım önerilmektedir.

Anahtar kelimeler: *sialolit; tükrük bezi hastalıkları; submandibuler bez*

Introduction

Sialolithiasis is one of the most common diseases of salivary glands[1]. Nearly 12 of every 1000 adults are referred to physicians with complaint of sialolithiasis[2]. Males are more frequently affected than females (2/1)[3]. It is observed in submandibular duct in 80% of the cases[4]. and is rarely bigger than 15 mm[1]. In 88 % percent of cases, it is smaller than 10 mm[4]. The term giant sialolith is used when the sialolith is over 15 mm or 1 gram[5,6]. Giant sialolithiasis of submandibular duct has been reported rarely[7]. We will discuss giant submandibular gland duct sialolithiasis in this report.

Case Report

A 55 year-old male patient complaining of intermittent pain and swelling in left submandibular area was admitted. Starting four months ago, the pain was increasing during chewing. The patient's past medical history was unremarkable.

On otolaryngologic examination, palpation revealed a swollen area corresponding to the anatomic location of submandibular salivary gland. The swollen area was palpated extra orally and intraorally, it was firm and nontender. A firm yellowish mass of approximately 4 cm × 1 cm on the floor of the mouth was determined (Figure 1). A lateral occlusal radiograph showed a large radioopaque calculus in the floor of the mouth (Figure 2).

Ultrasound revealed a giant stone in the submandibular area. Biochemical and serological studies were unremarkable.

The calculus was excised via transoral sialolithotomy under local anesthesia (Figure 3). Amoxicillin-clavulanic acid, 1 gram twice a day, and ketoprofen twice a day were used till the post operative seventh day. The symptoms resolved following operation. There was no recurrence and complication in the sixth month of the follow up.

Discussion

Sialolithiasis occurs after the obstruction of the salivary glands or ducts[8]. Mechanism of the calculus formation is not understood completely, however there are some theories.

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Figure 1. *Sialolith protruding from the Wharton duct.*

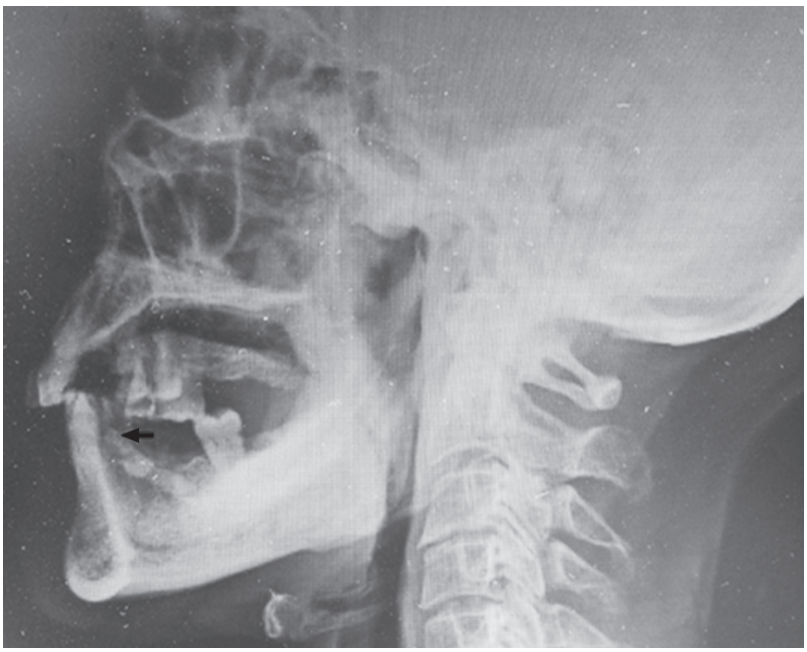

Figure 2. *The opacity at the floor of the mouth is shown in lateral cervical X-Ray graphy (black arrow).*

Figure 3. *Sialolith following excision.*

According to Harrison, micro calculus occurs in some instances, however it is excreted out of the natural ostium of the gland. Certain conditions causing changes in the chemical composition of the saliva, secondary to the partial or complete obstruction of the duct may increase the size of the calculus[9]. Depending on an alternative theory the mucous plaque forms a nidus and leads to the formation of calculus. The nidus increases with the accumulation of inorganic substances[10].

The flow of the saliva is contrary to the gravity, thus, about 80% of sialolithiasis is encountered in submandibuler gland or duct, though the Wharton's duct is longer and wider as the Stensen's duct[4].

The saliva in submandibular gland is more alkaline. Submandibular gland has mucinous secretion which is rich of protein, calcium and phosphate[11]. An experimental study showed that the magnesium content of the saliva secretion is the main factor for calculus formation[12].

Giant sialolith is defined when it is over 1 gram or 15 mm[5,6]. The calculus we excised was about 25 mm. Giant sialolithiasis usually has a dense concentration and a yellowish color. It is radio-opaque and sometimes interferes with teeth[1]. The symptoms include pain and swelling during eating secondary to the distension in the gland[1]. If the calculus dilates the duct, it does not hinder the flow of the saliva. Thus, it may become giant without any symptom[13].

Standard mandibular occlusal graph is the best diagnostic option to determine the calculus in the duct[7]. Sialography, ultrasonography and computerized tomography may help in diagnosis[14]. We identified the radio-opaque calculus with the aid of the radiologic image.

Sialolithiasis rarely may associates with salivary gland tumors. Hasegawa et al. and Batzakakis et al. reported a case associated with adenoid cystic carcinoma[15,16]. Sialoendoscopy is a new technique used in the diagnosis and treatment of sialolithiasis and it properly locates the stone[17,18]. However its use is limited in sialolithiasis over 6 mm and in case where the sialolithiasis is originated from the wall of duct[18-22]. Despite the fact, Wallace et al. excised successfully a giant submandibular gland and duct sialolith with sialoendoscopy. Sialolith was found at the gland in six cases and at the duct in one case. They could save the submandibular gland in 86% of the cases and concluded that the sialoendoscopy might be used successfully in sialolithiasis of submandibular glands and ducts[17]. Trans-oral sialolithotomy is usually performed for the sialolithiasis palpated easily at the floor of the mouth[17].

Submandibular stones can be removed surgically by intra or extra oral approach[17]. The choice of the treatment depends on the stone's location. Intraoral approach is often used when the calculi is located anterior to the lingual nerve and artery. The complications of intraoral surgery are lingual nerve anesthesia and injury. The lingual nerve loops around the distal portion of Warthin's duct. Excision of the submandibular gland by an external approach carries a risk of marginal mandibulary nerve palsy in 0-8% of the cases[17]. Shock wave lithotripsy, basket retrieval, and endoscopic laser lithotripsy are new treatment opsions[22]. A review found that the retrieval of stones by baskets or micro forceps was usually performed for stones less than 5 mm and extracorporeal lithotripsy was mainly used for fixed parotid stones less than 7 mm in diameter[23]. We excised the calculus via transoral sialolithotomy. Normal saliva flow must be maintained during treatment. Minimal invasive surgery is the recommended surgical option.

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Coronary Vasospasm Due to 5-Fluorouracil Treatment: A Case Report

5-Flourouracil Tedavisine Bağlı Koroner Vazospazm: Bir Olgu Sunumu

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ABSTRACT

5-Fluorouracil is the key chemotherapeutic agent used in the treatment of adenocarcinomas of the gastrointestinal system. However, serious cardiac side effects related to 5-fluorouracil treatment including coronary vasospasm, thrombosis, myocardial infarction, cardiomyopathy and sudden death have been reported previously. The incidence of cardiotoxic effects depends on the dose and route of application.

In this case report, a coronary vasospasm mimicking anterolateral myocardial infarction due to 5-fluorouracil-induced cardiotoxicity was presented.

It must be kept in mind that 5-fluorouracil may cause coronary vasospasm mimicking acute myocardial infarction and the situation can be treated successfully with nitrates and calcium channel blockers.

Key words: *acute coronary syndrome; cardiotoxicity; coronary vasospasm; 5-fluorouracil*

ÖZET

5-Fluorouracil gastrointestinal sistem adenokarsinomlarının tedavisinde anahtar kemoterapotik ajandır. Bu ajanın, koroner vazospazm, tromboz, miyokard infarktüsü, kardiyomyopati ve ani ölüm gibi ciddi kardiyak yan etkileri bildirilmiştir. Kardiyotoksik etki görülme sıklığı doz ve veriliş yoluna göre değişmektedir.

Burada 5-fluorouracil kardiyotoksisitesinin neden olduğu anterolateral miyokard infarktüsünü taklit eden bir koroner vazospazm olgusu sunulmuştur.

5-Fluorouracil uygulamasının akut miyokard infaktüsünü taklit eden koroner vazospazma neden olabileceği ve bu durumun nitrat ve kalsiyum kanal blokerleri ile başarıyla tedavi edilebileceği akılda tutulmalıdır.

Anahtar kelimeler: *akut koroner sendrom; kardiyotoksisite; koroner vasospazm, 5-fluorouracil*

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Introduction

5-Fluorouracil (5-FU) is a pyrimidine antagonist chemotherapeutic agent. It is frequently used in the treatment of gastrointestinal, breast, head and neck tumors and has cardiotoxic effects. Angina pectoris, acute myocardial infarction, supraventricular and ventricular tachycardia, coronary dissection, congestive heart failure, cardiomyopathy, myopericarditis, cardiogenic shock and sudden death are most serious cardiac side effects[1,2]. The frequency of cardiotoxicity is reported to be between 1.2- 18%[3]. The underlying mechanisms of cardiotoxicity have not been fully understood yet, however many mechanisms including the coroner vasospasm have been suggested for its cardiotoxic effects[4].

In this report, we presented a case of coronary vasospasm occurred during 5-FU infusion as a component of oxaliplatin, folic acid and altuzan (FOLFOX-6-Altuzan) chemotherapy regimen given for the treatment of colonic adenocarcinoma.

Case Presentation

A 50 year old woman was referred to our intensive care unit with the suspicion of a myocardial infarction. 5- FU, oxaliplatin, folic acid and altuzan (FOLFOX-6- Altuzan) protocol was started 28 days ago with the diagnosis of colon cancer.

The woman developed typical angina pectoris at rest during regimen infusion. The therapy was discontinued and the patient was transferred to our intensive care unit because the electrocardiogram (ECG) showed ischemic changes. The first ECG showed ST elevation and peaked T waves in D_{I-III}, aVL, aVF and V_{2-6} derivations as well as reciprocal changes in aVR and V_I

(Figure 1). Detailed history revealed that a coronary angiography revealing non-pathological findings was performed two weeks ago as a result of a similar clinical picture in another center.

The chest-pain resolved following the administration of nitroglycerin (5-100 mg/min) and diltiazem, and the ECG findings improved rapidly (Figure 2). The transthoracic echocardiography and consecutive control of CK- MB (normal levels; 14-16 U/ L) and troponine T (normal levels; 0.002- 0.24 ng/ml) measurements revealed normal findings. Other probable causes of chest pain like pericarditis, hyperventilation and alkolosis were ruled out and the case was diagnosed as a coronary vasospasm due to 5-FU treatment.

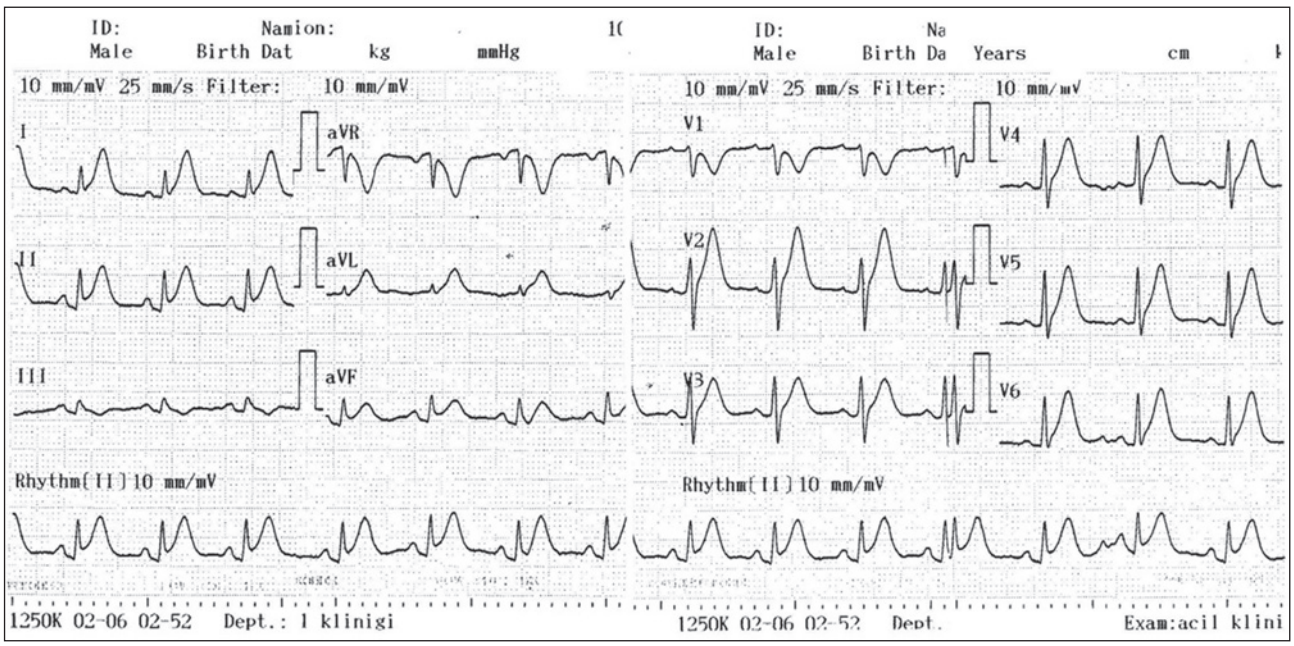

Figure 1. *The Electrocardiogram on admission showing sinus rhythm with ST-segment elevation in the derivations of DI, DII, DIII, aVL, aVF and hyperacute T wave changes in the derivations of V2 to V6.*

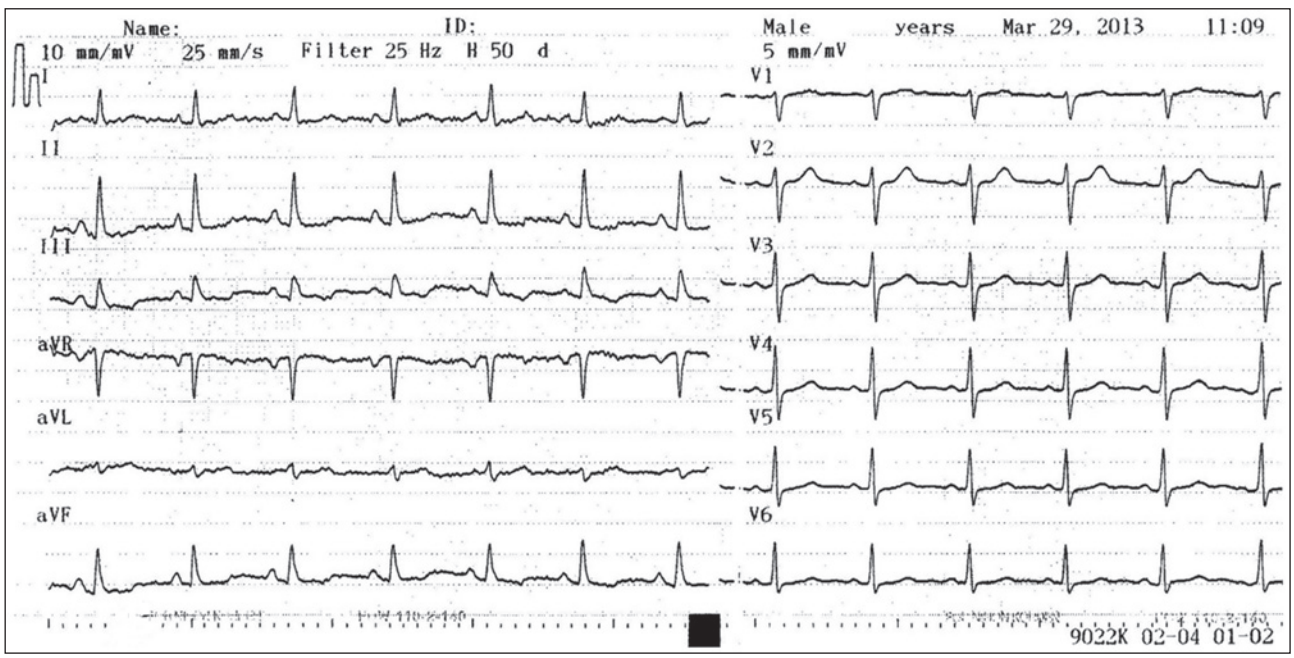

Figure 2. *The Electrocardiogram of the patient after the pain resolved whit nitrate and calcium canal blocker treatment.*

The woman was discharged on the next day and her chemotherapy protocol was modified. In the course of follow up, the patient was free of chest pain with the modified chemotherapy regimen.

Discussion

This case was presented to underline the cardiotoxic side effects of 5- FU and the importance of getting a detailed patient history before emergency primary percutaneuos angioplasty.

Although the mechanism of cardiotoxic effects of 5-FU is not clear, coronary artery spasm, autoimmune-mediated injury of the myocardium, endothelial damage, thrombogenic effects or thrombus formation, direct myocardial toxicity causing necrosis and accumulation of metabolites have been suggested to play a role[4]. The most frequently suggested mechanism is the coronary vasospasm caused by 5-FU itself or its metabolites (fluoro beta alanine and fluoro acetate).

In ultrasonographic and angiographic studies, 5-FU infusion has been shown to cause vasospasm in both the coronary and the brachial arteries. Vasospasm is a reasonable mechanism, since it would explain reports of the efficacy of vasodilating drugs given prophylactically to patients who experienced a previous episode of chest pain during 5-FU treatment[5,6].

Angina pectoris, acute myocardial infarction, congestive heart failure, cardiomyopathy, myopericarditis, ventricular and supraventricular tachycardia, prolonged QT interval, sudden death, cardiogenic shock and coronary dissection are counted among cardiotoxic effects of 5-FU[2]. Angina pectoris occurred during or after 5-FU administration is the most common symptom. Kounis syndrome, which can be described as the syndrome of allergic angina and allergic myocardial infarction, and Tako-Tsubo cardiomyopathy cases related to 5-FU were also reported[7-9].

It was reported that the reversible angina continued up to 12 hours after the cessation of 5-FU in 19% of cases and recurred in 90% of patients following readministration[10]. For this reason, it is recommended to stop 5-FU and replace it with another chemotherapeutic agent in case of cardiotoxicity.

The incidence of cardiotoxic effects changes depending on the dose and route of application. It was reported between 1.6–3% with earlier bolus regimens, however increased up to 7.6–18% with prolonged infusion regimens[10]. Higher doses (>800 mg/m^2) and continuous infusions increased the incidence of cardiotoxic side effects. A complete cardiovascular evaluation, close follow up, monitorization and prophylactic calcium channel blockers and nitrate administrations are suggested for every patient receiving 5-FU infusion[11].

In conclusion, 5-FU is the key chemotherapeutic in colonic adenocarcinomas, however its cardiovascular side effects should not be ignored. The incidence of these side effects increase with higher doses and continuous infusions. In case of a cardiovascular event, the chemotherapeutic regimen should be modified and 5-FU should not be used again. It must be kept in mind that 5-FU administration may cause coronary vasospasm mimicking acute myocardial infarction and the situation can be treated successfully by nitrates and calcium channel blockers.

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AMAÇ VE KAPSAM

Kafkas Tıp Bilimleri Dergisi (Dergi) Türkçe ve İngilizce yazılmış makaleleri kabul eden, hakemli bir genel tıp dergisidir. Dergi tıbbi bilimleri geliştiren ve aydınlatan ya da okuyucularını eğiten orijinal biyomedikal makaleleri (Tıp bilimleri ile ilgili araştırma, kısa bildiri, derleme, editöryal, editöre mektup, çeviri, tıbbi yayın tanıtma vb türlerden yazılar) yayımlar. Yılda 3 sayı halinde (Nisan, Ağustos, Aralık) tek cilt olarak, matbu ve elektronik ortamlarda basılır. Dünyanın her yerinden makaleler kabul edilir.

MAKALE GÖNDERME

Makale toplama ve değerlendirme işlemleri http://meddergi.kafkas.edu.tr web adresinden online yapılır. Web adresinden giriş yapılmasını takiben "online makale gönder, takip et, değerlendir" butonunun tıklanması ile çıkacak direktiflerin takip edilmesi gereklidir.

ETİK

Dergi, Yayın Etikleri Komitesi'nin (COPE) rehberlerindeki iyi yayın uygulamaları ilkelerine sıkı bir şekilde bağlıdır (http://publicationethics.org/resources/guidelines). Makale başvurusunda bulunan yazarlar; çalışmalarının etik, hukuki ve bilimsel kurallara uygun olduğunu, daha önce yayınlanmamış ve başvuru sırasında başka bir yerde yayınlanmak için değerlendirme aşamasında olmadığını kabul ederler. Daha önce yayınlanmış tablo, şekil ve yazı makalede açıkça belirtilmeli ve yayın haklarını elinde tutanlardan izin alınmalıdır. Dergi, uygun etik kurul başvurularının yapılmış olmasını, bilgilendirilmiş onamların alınmasını ve bunların makalede bildirilmesini zorunlu tutar. İnsan öğesini içeren tıbbi çalışmalarda, Helsinki Deklarasyonu ilkelerine sıkıca bağlıdır (http://www.wma.net/e/policy/pdf/17c.pdf). Yazarlar, laboratuvar hayvanlarının kullanımında ve bakımında kurumsal ya da ulusal rehberlere uygun davrandıklarını bildirmek zorundadır.

BAŞVURU SIRASINDA İSTENEN MAKALE NİTELİKLERİ

Dergi, Uluslararası Tıp Dergileri Editörleri Komitesi'nin (ICMJE) rehberlerine sıkıca bağlıdır (http://www.icmje.org/index.html). Türkçe makaleler için, Türkçe özete ek olarak İngilizce özet; İngilizce makaleler için, İngilizce özete ek olarak Türkçe özet istenmektedir.

MAKALE HAZIRLANMASI

Tercihen Times New Romans yazı karakteri, 12 punto ve çift aralıklı yazılması önerilir. Makaleler açık, kısa ve akıcı bir Türkçe veya İngilizce ile yazılmalı, imla kurallarına uyulmalıdır. Dergi, özellikle giriş ve tartışma kısmı olmak üzere, makale uzunluğunu içerdikleri bilgiyle orantılı ölçüde kısa tutulmasını önerir. Bütün yazarlara bir istatistik uzmanı ile görüşmeleri önerilir.

Başlangıç Sayfası: Makale başlığı kısa ve devamlı nitelikte olmalıdır. Başlık indeksleme ve bilgi toplama açısından yararlı olacak biçimde tanımlayıcı ve bilgi verici olmalıdır. Bütün yazarların ad ve soyadları yazılmalıdır. Her yazar için çalıştığı bölüm, kurum belirtilmeli, iletişim yazarının şehir, ülke ve posta kodunu da içeren tam yazışma adresi, fax, telefon ve Email adresi sunulmalıdır.

Özet: Özetler anlaşılır olmalı ve yazının amaç ve belirgin sonuçlarını gösterebilmelidir. Yalnızca temel bulgu ve sonuçları belirterek, uyarlanmaya gerek duymadan özetleme servislerince kullanılabilmelidir. Araştırma makalelerinde özet bölümü yazısını şu alt başlıklara (Giriş, yöntem, bulgular, sonuç) göre sıralamak gerekir. Derlemeler,olgu sunumlarında alt başlık gerekmez. Editöryal, editöre mektup gibi türlerde özetleme yapılmaz. Özetlemede yalnızca standart kısaltmalar kullanılmalıdır.

Anahtar Kelimeler: Yazıyla ilgili "Index Medicus: Medical Subject Headings ve Türkiye Bilim Terimleri" standartlarına uygun üç ile altı arası anahtar kelime özet altına yazılmalıdır.

Giriş: Anlaşılır ve kısa olmalı, son paragrafında çalışmanın amacı açıkça belirtilmelidir. Literatürün gözden geçirilmesi çalışmanın nedenselliğine yönelik olmalı ve önemli bilgileri içermelidir.

Yöntem: Gözlemsel ya da deneysel çalışma katılımcılarının neye göre seçildiği (hastalar, kontroller ya da laboratuvar hayvanları) açıkça tanımlanmalıdır. Katılımcıların yaş, cinsiyet ve diğer önemli özellikleri belirlenmelidir. İnsan ve hayvanlar üzerinde yapılan çalışmalarda etik standartlar açıkça tanımlanmalıdır. Yazarlar, diğer araştırmacılar tarafından da bulguların tekrarlanabilmesi için yöntem, cihaz ve işlemleri yeterli açıklıkta tanımlamalıdırlar. İstatistiksel yöntemler de dahil, daha önceden kabul görmüş yöntemler için referanslar sağlanmalıdır. Yeni ya da uyarlanmış eski yöntemler tanımlanmalı, neden kullanıldıkları ve sınırları açıklanmalıdır. Bütün ilaç ve kimyasallar jenerik isimleri, dozları ve uygulanma yolları sunulmalıdırlar. Randomize kontrollü klinik çalışmalarda, çalışmanın ana öğeleriyle ilgili, çalışma protokolü (çalışma populasyonu, müdahaleler ya da maruziyetler, beklenen sonuçlar ve istatistik analizin nedenselliği), müdahalelerin belirlenmesi (randomizasyon yöntemi, gruplara ayırmada gizlilik) ve grupların maskelenmesini (körleme) içeren özellikler sunulmalıdır. Yapılan istatistiksel analiz yöntemi belirtilmelidir. Makalenin anlaşılması için özellikle gerekli değilse, istatistiksel testlerin ayrıntılarla anlatılması gerekmez. Ancak, özellik arz eden yöntemler kullanıldığında ve makale istatistik ağırlıklı olduğunda ayrıntılı tanımlar gereklidir.

Bulgular: Tablo, şekil ve yazıda sunulan bilgilerin gereksiz tekrarlanmasından kaçınılmalıdır. Yalnızca tartışma ve ana sonucun anlaşılması için gerekli olan önemli bilgiler sunulmalıdır. Veriler bütünlük içinde ve tutarlı olarak sunulmalı, raporun açık ve mantıksal ilerlemesi sağlanmalıdır. Tablo ve şekillerdeki veriler yazıda tekrarlanmamalıdır. Yalnızca önemli gözlemler vurgulanmalı ya da özetlenmelidir. Aynı veriler hem tablo hem de grafiklerde sunulmamalıdır. Verilerin yorumlanması tartışma bölümüne saklanmalıdır.

Tartışma ve Sonuç: Tartışma asıl bulguları anlatan kısa ve özlü bir cümle ile başlamalı, çalışmanın güçlü ve zayıf yönlerini tanımlamalı, bulguları diğer çalışmalarla ilişkilendirerek tartışmalı, olası açıklamalar sağlamalı ve gelecekte yanıtlanabilecek sorulara işaret etmelidir. Tartışma, bulgular bölümünde zaten sunulmuş bulguların tekrarıyla değil, bunların yorumlanmasını ile ilgilenmelidir. Yeni bulgularla, zaten bilinenlerin ilişkisini kurmalı ve mantıksal çıkarsamalar yapmalıdır. Sonuç çalışmanın amacıyla ilişkilendirilebilir ama niteliksiz önermelerden ve verilerle desteklenmeyen sonuçlardan kaçınmak gerekir. Çalışmanın üstünlüğü konusunda iddialarda bulunmaktan kaçınmak gerekir. Öneriler kesinlikle gerekli ve konuyla ilintiliyse tartışma bölümünde belirtilmelidir.

Teşekkürler: Teşekkürler kısa ve net olmalı, yalnızca bilimsel/teknik destek ve finansal kaynak için yapılmalıdır. Rutin kurum olanaklarının kullanılması, makale hazırlanmasındaki destek ya da yardımlar (yazma işi ya da sekreterlik işleri) gibi durumları içermemelidir.

Kaynaklar: Normalde toplam kaynak 30 adet ile sınırlandırılmalıdır. Literatüre atıfta bulunan kaynaklar ardışık olarak sıralanmalı ve makalenin sonunda yer almalıdır. Yazının bütününde atıflar üst karakterle cümle bitiminde yer almalıdır. Olabildiğince yazı içinde yazar isimleri kullanmaktan kaçınmak gerekir. Kafkas Tıp Bilimleri Dergisi aynı zamanda ulusal dergilerin kaynak gösterilmesini teşvik eder. Kaynaklar; Index Medicus stiline uygun yapılmalıdır. *Üç yazarlıya kadar makale:* Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV-infected patients. N Engl J Med 2002; 347:284-7. *Üçten fazla yazarlı makale:* Rose ME, Huerbin MB, Melick J, et al. Regulation of interstitial excitatory amino acid concentrations after cortical contusion injury. Brain Res 2002; 935:40-6. *Kitap:* Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002:93-113.

Tablolar: Tablolar ayrı olarak yazılmalı ve verilen rakamlar ile sıralanmalıdır. Her tablo kendisi ile ilgili tanımları içermeli ve kısa tanımlayıcı başlık içermelidir. Tablo içindeki kısaltmalar, tablo altında açıklanmalıdır. Tablo (ilgili başlık, tanımlayıcı ve açıklayıcı bilgiler) ayrı bir sayfada sunulmalıdır.

Şekiller: Şekiller (ilgili başlık, tanımlayıcı ve açıklayıcı bilgiler) ayrı bir sayfada sunulmalıdır.

MAKALE DEĞERLENDİRME SÜRECİ

Dergiye sunulan bütün yazılar en az iki hakem tarafından değerlendirme işlemine alınır. Karar hakem değerlendirme raporlarına göre verilir. Bütün kabul görmüş makaleler dergi kural ve formatına uygun olarak redaksiyon işlemine tabi tutulur.

SON KONTROL

Yazının kabulünü takiben yapılacak editöryal işlemlerden sonra, yazının mizanpajlı şekli yazarların onayına sunulacak ve üç gün içinde telif hakkı devir formu ile birlikte geri istenecektir.

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Kafkas Tıp Bilimleri Dergisi'ne yazı teslimi, çalışmanın daha önce hiçbir yerde yayımlanmadığı (özet şeklinde ya da bir sunu, inceleme ya da tezin bir parçası şeklinde yayımlanması dışında), başka bir yerde yayımlanmasının düşünülmediği ve Kafkas Tıp Bilimleri Dergisi'nde yayımlanmasının tüm yazarlar tarafından uygun bulunduğu anlamına gelmektedir. Yazar(lar), çalışma ret edilmedikçe, yazıya ait tüm hakları Kafkas Üniversitesi ve Kafkas Tıp Bilimleri Dergisi'ne devretmektedir(ler). Yazar(lar), Kafkas Üniversitesi ve Kafkas Tıp Bilimleri Dergisi'nden izin almaksızın çalışmayı başka bir dilde ya da yerde yayımlamayacaklarını kabul eder(ler).

DOI NUMARASI

Yayımlanan her bir makaleye dijital nesne tanımlayıcı numarası (doi) atanır.

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Keywords: Between three and six keywords that are suitable with "Index Medicus: Medical Subject Headings and Turkish Scientific Terms" standards should be written under abstract section.

Introduction: Introduction should be brief and state precisely the scope of the paper. Review of the literature should be restricted to reasons for undertaking the present study and provide only the most essential background.

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